ARCHIVES OF SURGERY

VOLUME 14 APRIL, 1927 NUMBER 4

INTRACYSTIC PAPILLOMATOUS TUMORS OF THE BREAST, BENIGN AND MALIGNANT

ANALYSIS OF ONE HUNDRED AND TWENTY-FOUR CASES *

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This breast tumor may now be considered as a distinct type made up of a cyst or dilated duct into which projects a soft, friable, papillomatous growth. In occasional cases in the same breast, or in the wall of the cyst, definite carcinoma is present with invasive and metastatic properties. In the literature the condition is referred to under various names—adenoma, villous papilloma, duct papilloma, cystadenoma papillae, polycystoma proliferum, proliferating cystadenoma, papillary cystoma, duct cancer and carcinome villeux. With these is often described another tumor of common occurrence, but one that only rarely takes a form that could be confused with the true papilloma. This growth shows a cauliflower-like projection into the cyst, rather than the soft, friable, delicate branchings of the primarily epithelial structure. It is referred to as cystadenoma intracanaliculare, intracanalicular cystadenoma or myxoma, and endocanalicular papillary fibroma. We have been accustomed to call this the intracanalicular fibro-adenoma or myxoma, and it seems to be primarily and predominantly a connective tissue growth. Two cases of this type of tumor are included in this series, for the reason that clinically and at operation they present a similar picture.

The result of this study, based on 104 benign and twenty-four malignant tumors and five cases with the diagnosis uncertain may serve (1) to emphasize the number of cases wrongly diagnosed as cancer; (2) to bring out the points of differential diagnosis between the benign and malignant forms, both clinically and at the exploratory operation, and (3) to present a method of attack that will give the patient the best chance of a correct diagnosis and proper treatment.

Furthermore, since the largest series of similar tumors heretofore reported has included about twenty cases, Deaver and McFarland basing their chapter in The Breast on forty compiled cases, and the literature being made up largely of small groups of individual reports, it is hoped that the study of this series will make a definite addition to the information available on this type of breast tumor.

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LITERATURE

In the reported cases there is throughout a relative consensus of opinion either that these tumors are malignant, but in a relatively low degree, or that, even if benign, they may undergo carcinomatous change. This fear has caused the surgeon to perform an extensive operation for their removal, after which he has given a good prognosis, since they were supposed to be "cancer of a relatively low grade of malignancy."

The early authors considered all these tumors as cancers, while the English writers, Williams,[1] Bryant,[2] Shield[3] and others, differentiated the benign, intracystic papillomas. However, there is still much confusion, and mistaken diagnoses, which class the benign cases as cancer, are still frequent.

Ewing[4] holds that malignant forms are relatively common, but says that the lymph nodes may remain immune for an indefinite period. Delbet thinks malignant forms are sufficiently common to justify radical treatment in all cases. According to Upcott,[5] from four to five out of every ten cases are malignant. Greenough and Simmons[6] class three out of their twenty cases as cancer. In one case clinically malignant, death from cancer followed a radical operation. In another, with nothing in the clinical report to suggest cancer, the patient was well one year after simple removal of the breast; the third patient, in whom the tumor was beneath the nipple and adherent to the skin, was well two years after removal of the breast alone.

Evans[7] says that a nipple discharge in a nonlactating breast is associated with a papillary growth, either intracystic, when it may be a "duct carcinoma," or protruding, when it is the less dangerous "duct papilloma." Murphy[8] reports a case in which there was a villous growth arising from an otherwise smooth-walled cyst. The cut surface of the solid portion of the tumor was encapsulated and apparently situated on the side of the cyst wall from which the papilloma arose. He believed the condition to be suggestive of a low grade of malignancy and treated it as carcinoma, dissecting out the axillary glands. In these no metas-

1. Williams, W. R.: A Monograph on Diseases of the Breast, Their Pathology and Treatment, with Special Reference to Cancer, London, J. Bale and Son, 1894.

2. Bryant, Thomas: The Diseases of the Breast, London, Cassell & Co., 1887.

3. Shield, A. M.: A Clinical Treatise on Diseases of the Breast, London, Macmillan Company, 1898.

4. Ewing, James: Neoplastic Diseases; a Treatise on Tumors, Ed. 2, Philadelphia, W. B. Saunders Company, 1922.

5. Upcott, H.: Practitioner **91**:14-18, 1913.

6. Greenough, R. B., and Simmons, C. G.: Ann. Surg. **45**:188, 1907.

7. Evans, J. H.: Practitioner **91**:7, 1913.

8. Murphy, J. B.: Surg. Clin., Philadelphia, **3**:569-574, 1914.

tases were found. Warren [9] gives a good prognosis after early and complete removal, stating that in recent cases removal of the breast or even of the tumor alone is all that is called for, but that without this the danger of malignant sequelae is very great.

Speese [10] cites two cases which from his report seem to be unquestionably benign. In one a radical operation was done on a girl of 22 years who had had a tumor for eight years. The other patient, aged 35, had only the tumor removed, this showing a cyst with a smooth wall except for one small, red, papillary projection. She refused to have a radical operation and was well eighteen months later. He doubts the diagnosis of malignancy in these two cases.

Our early records are in accord with the prevailing opinion expressed in the literature concerning the nature of these tumors. In the histories of cases now diagnosed as benign there are repeated pathologic reports of malignancy, but with a good prognosis "since this type of cancer metastasizes relatively late." The later records likewise impress on us the present day, widespread persistency of fear of malignancy in these tumors: many of the specimens that were received with a provisional diagnosis of cancer have, after a careful study, been placed in the benign group. Three recent striking examples of this may be cited. In the first a girl of 16 had both breasts removed because of a bloody nipple discharge and a microscopic diagnosis of cancer. In the second, a girl of 22, with a history of a tumor of two years' duration, clinically benign, had the entire breast removed after the tumor had been excised and found to contain bloody fluid. In the third case a diagnosis of "cancer cyst" was made, despite the fact that the tumor, as described by the surgeon, was encapsulated.

ANALYSIS OF CASES INCLUDED IN THIS REPORT

Method of Investigation.—At the beginning of this study each case was carefully worked over pathologically, grossly when the material was available, and microscopically in every case. Where there was a question of changing the diagnosis, the correctness of this revision was made more certain by including in this restudy the sections on which the original classification had been made. These cases were then referred to Drs. Bloodgood and MacCallum, and no changes were made without their joint approval. No mistaken diagnoses were found in the benign group, but ten cases, in addition to quite a number already reclassified as benign, had to be removed from the malignant group. Four of these were classed as unquestionably benign (under report of cases). Five

9. Warren, J. C.: The Surgeon and the Pathologist, J. A. M. A. **45**:149 (July 15) 1905.

10. Speese, J.: Ann. Surg. **51**:212, 1910.

were placed in a special group with the diagnosis questionable: one early case because of a lack of microscopic confirmation of the gross diagnosis; in the other four because there was a difference of opinion (under report of cases). Still another early case showing a cancer cyst had to be removed from the malignant group, since it was a squamous cell carcinoma and apparently had arisen from a dermoid cyst.

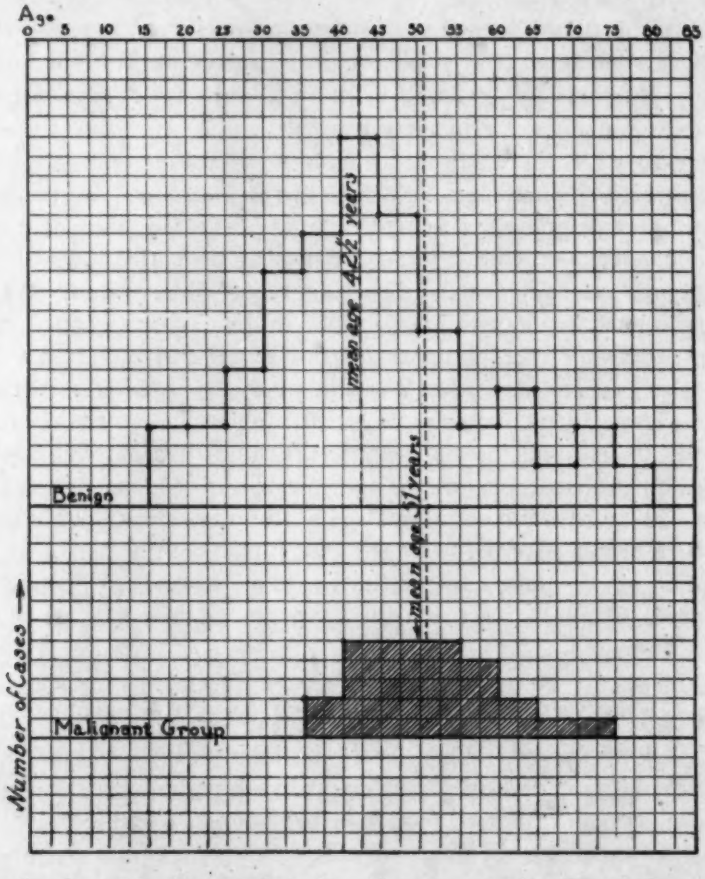

Fig. 1.—Age at onset: actual number of cases occurring in each five year age period. The mean age for the benign group is seen to be 42½ years; for the malignant group 51 years. This chart also shows the large number of benign tumors occurring in patients under the cancer age. Benign group, light; malignant group, shaded; two squares represent one patient.

BENIGN GROUP

The following is a composite picture based on ninety-five cases, with a second operation for a similar tumor in nine, giving a total of 104 reports.

History.—In general these tumors occurred in women of any age after puberty, but most frequently between 20 and 65, with 4 per cent under 20 (fig. 1). The complaint was of a lump in the breast in seventy-five cases and a discharge from the nipple in sixty-nine cases, the two conditions being frequently associated. In twenty cases there was a history of the discharge alone; in ten of these patients a tumor was present on examination and the remainder had the operation performed solely for the bloody discharge. In eighteen patients with a complaint of a lump in the breast there was no history of a nipple discharge.

Type of Discharge.—The discharge was bloody in forty one cases, serous in eight, and varying between bloody and serous in seven. In one it consisted of green pus. In several cases there is no note as to its character. It was usually intermittent, sometimes with a complete cessation for a considerable time, while in other cases it occurred daily, and in a few it was present almost constantly. There were a striking number of reports in which it was noted only, or was more marked, at night, this condition probably being due to the position of the patient causing pressure on the breasts. The usual story was that of a gradual growth, but a few patients had noted a rapid increase in size, associated with pain, and either a cessation of the discharge or tenderness, redness and evidence of infection. Four of the tumors had ruptured with a discharge of a bloody material, in one case on three occasions, and three of the patients came in with a persisting sinus and a purulent discharge. (Greenough and Simmons report a case with a sinus.)

Cessation of Discharge.—There are sufficient data to establish the fact that in these tumors with a cessation of the discharge there is frequently an increase in the size of the tumor. It becomes more tense and painful, and the pain is relieved by the reappearance of the nipple discharge, the tumor at the same time decreasing in size and becoming softer in consistency. There was a definite history of seven tumors decreasing in size, five disappearing entirely for a variable period of time, in two with a known associated discharge of material from the nipple.

Onset.—The first thing noted was the discharge from the nipple in forty-seven cases, a tumor in thirty-seven, and pain in thirteen. The pain in five instances caused the patient to discover the tumor.

Duration of Symptoms.—The duration varied for the decades since our first recorded cases as follows: Those since 1920 had an average duration of 1.76 years, increasing with each decade back to the earliest cases between 1895 and 1900 when the average duration was 4.75 years (fig. 2). The total number of patients falling in any period of duration from a few days to twenty-five years can be seen at a glance in fig. 3. Eighteen of the patients had had symptoms for five years or more. The

duration of the tumor, nipple discharge and pain ran parallel courses, the number of patients with these symptoms decreasing for the periods of longer duration (fig. 4). The only two variations from this were that ten of the tumors were discovered on physical examination, and the fact that the number of patients with pain falls more rapidly for the periods of longer duration. Only five patients had had pain for more than two years, and none for more than ten years, while the discharge and tumor had been present at times for as long as twenty-five years, with ten and fifteen patients, respectively, giving a history extending over a period of more than two years.

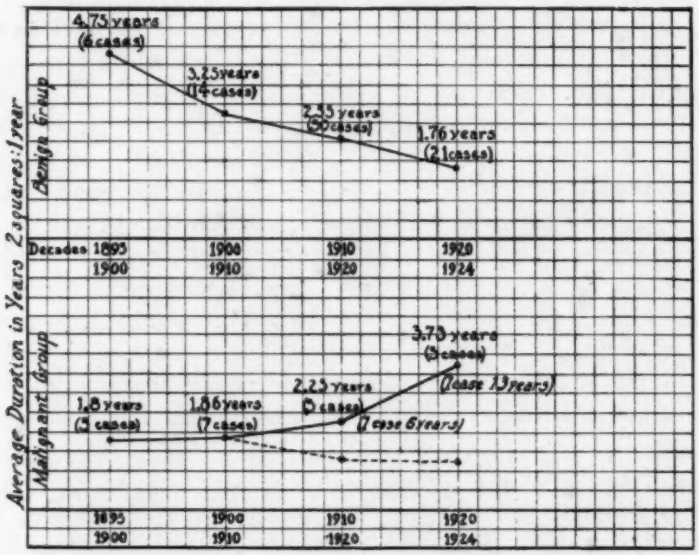

Fig. 2.—Known duration of lesion before operation, showing average duration in years for the cases occurring in each decade; in parentheses are given the number of cases on which this average is based. For the benign group, with the larger number of cases, there is a gradual fall in this curve from the first to the most recent cases. For the malignant group there is a recent increase in the average duration, but this can be seen to be due to one case of long duration in each of the last two age periods. There are so few cases for each decade in this group that the value of these statistics is questionable. Two squares represent one year. Dotted line shows slight fall of duration of cancer cases for recent years if the two cases of six and thirteen years' duration are not included.

Physical Examination.—In general the lesion occurred in white women,[11] (two cases in men and eleven in negro women) with predominantly single tumors, (sixty-two of seventy-five cases noted), the

11. In the laboratory the specimens from white predominate over those from colored patients. The exact ratio is difficult to determine.

majority of which were small, but with 38 per cent of those with the size noted being as large as an egg, base-ball, orange, grape-fruit, or more than 6 cm. in diameter. In an occasional case there were similar tumors in both breasts, and 15 per cent of these patients, either at the first examination or later, showed a similar condition in the other breast.

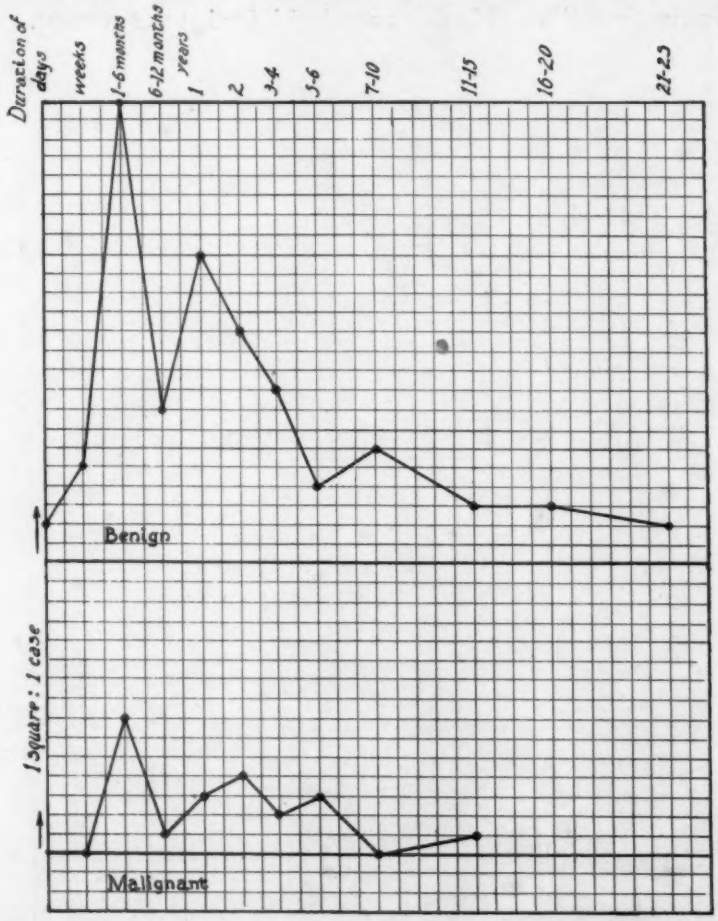

Fig. 3.—Duration of cases before operation: the relatively large number of benign cases of many years' duration, and with only one cancer case present over so long a period of time as to suggest that there has been malignant change in an old benign tumor, should be noted.

Location.—As a rule the tumor is in the central part of the breast, thirty-seven of the forty single or small tumors, with the location noted, being in this situation (fig. 5). In eight other cases it occupied the greater part of the breast, or there were multiple growths through the gland. In forty-eight cases the site was located by quadrants and not with reference to nipple or periphery.

Consistency.—The tumor was noted as soft or cystic in twenty-nine cases, tense in two, encapsulated in five, and as firm, nodular or shotty in thirty-two. The term "indurated" was used for seven, and "hard" or "hard, like cancer" for two.

Mobility.—In forty-two cases the growth was movable; it was fixed in only one (case 4), and in that a marked infection was present.

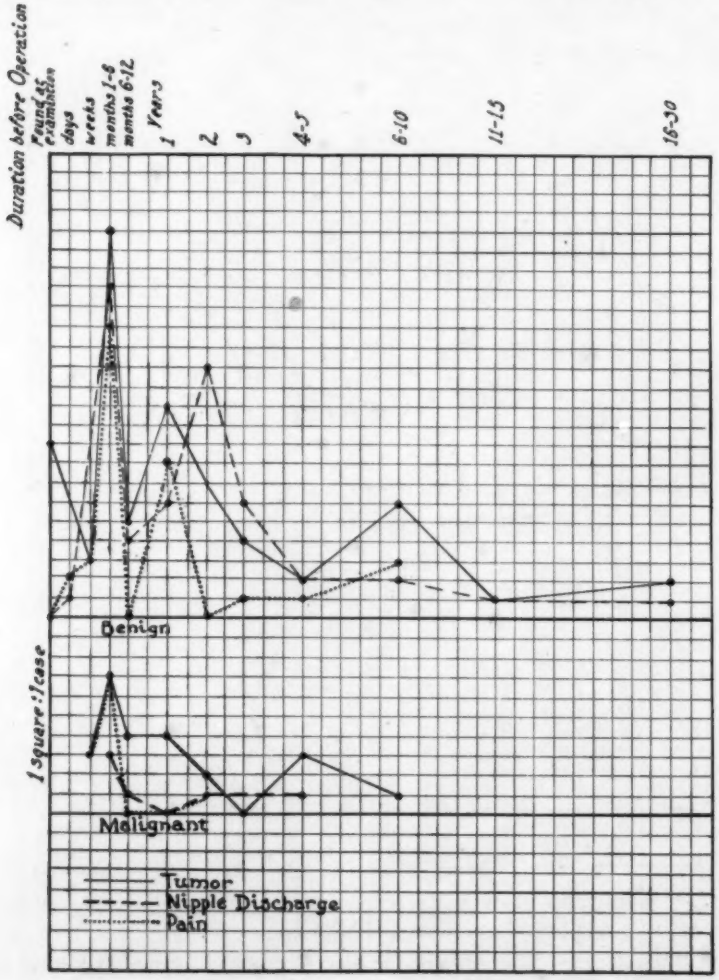

Fig. 4.—Duration of the growth of the tumor, nipple discharge and pain with the number of cases for each period. It will be noted that these run a somewhat parallel course, except that the number of cases with pain decreases more rapidly for the periods of longer duration, and that nipple discharge is much less prominent in the cancer than in the benign group.

Nipple.—In forty-three cases the nipple was noted as normal; in twelve, there was slight retraction; in three, it was protruded, and in

two obliterated. Here again these last two cases showed marked infection (case not reported here and case 4).

Skin.—The skin was normal in fifty cases, showed a sinus from rupture in three, was tense, thin or red over the tumor in five, and had dilated veins in one. There were slight changes, either dimpling, fixation or

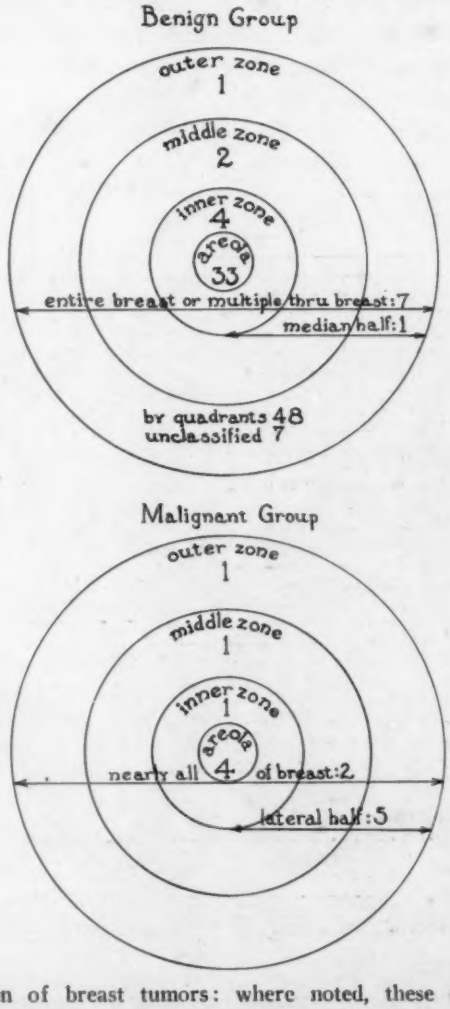

Fig. 5.—Location of breast tumors: where noted, these are predominantly tumors of the central part of the breast, but occasionally in the benign group they are multiple throughout the gland; in the malignant cases they are more frequently large enough to involve the greater part of the breast.

suggestive pig-skin appearance in nine, definite dimpling in two cases. In one of these infection was apparent, but with the section which we have of the other no diagnosis as to infection can be made. No history is given.

Lymph Glands.—In sixty-four cases the lymph glands were negative; in nine palpable, and in only one case (case 4, infected) were they hard and suggestive of malignancy.

Pathologic Examination.—The specimens and histories as received in the laboratory show that in 22 per cent the tumor only was removed; in 40 per cent the breast without the axillary contents or pectoral muscles; and in 38 per cent the radical operation for cancer was performed. In many cases (more than 50 per cent) in the last two groups exploratory incisions had been made.

The tumors were noted as single in 63 per cent of the cases, and multiple in 37 per cent. The size has already been given fairly accurately under the physical examination.

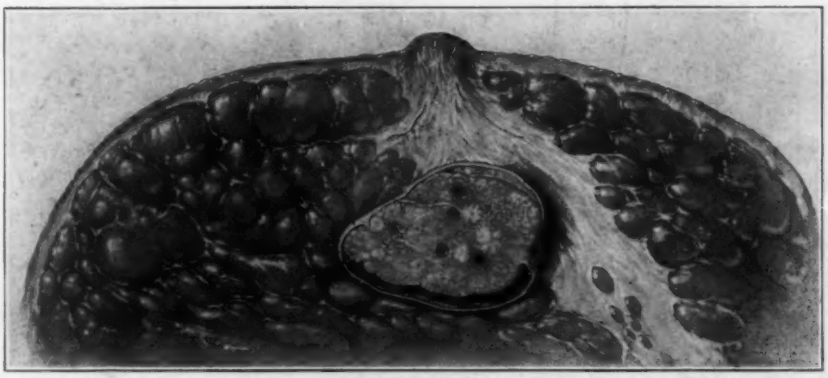

Fig. 6.—Ultimate results in the benign and malignant groups: among sixty-six cases of the benign group, followed for from one to twenty-two years, there were no deaths from tumor or recurrence, and relatively few deaths from any cause; in the malignant group, on the other hand, can be seen the high mortality from recurrence, only three patients being alive at the present time.

Section through the tumor showed a cyst, which was filled with a papillomatous mass in 3 per cent of the cases; in the remainder it contained fluid and one or more papillomas (fig. 6). The fluid was bloody in 83 per cent of the cases noted; in 11 per cent it was clear, and in one case each the cyst was filled with green pus, grumous material and cloudy fluid. Of the twenty-nine cases with no note on the cyst fluid, the nipple discharge was bloody in eight cases, watery in two, and green and yellow in one each; the type was not noted in three; in seven there was no discharge, and in seven there was no note. In three of the other ten cases in which the fluid was clear or amber, there was a history of a bloody discharge at some time; in three, a yellow or serous discharge; in three others, no discharge, and in one there was no note.

After the fluid had been evacuated the cysts were found to contain amounts of papillomatous growth varying from a small mulberry-like projection at one point in a large, smooth-walled cavity, to a cyst with a shaggy wall due to numerous, small papillomas, which occasionally completely filled the cyst. Ten patients were operated on for a bloody nipple discharge alone, and showed, either on gross or microscopic examination, a small papilloma projecting into a dilated duct.

Fig. 7.—Benign papillomatous cyst with the papilloma almost filling the cyst and appearing as a solid growth. There are few points of attachment; the thickening of the wall at one place is due to the closely attached papillomatous growth. The entire freedom of invasion, the loose attachment of the wall to the surrounding tissue, and the location beneath the nipple should be noted.

In a few cases, two of which are included in this series, there was a cauliflower-like growth projecting into the cyst. This clinically and at exploratory incision is often confused with the predominantly epithelial type of tumor. On microscopic examination, however, it showed the large projections to be the typical intracanalicular fibro-

adenoma or myxoma (fig. 17 and cases 10 and one case not reported here).

The wall of the cyst was not infiltrated in fifty cases; it was thick in two, but in no case is infiltration recorded (fig. 6). In most cases it is stated that the wall was thin, freely movable over the surrounding tissue, and with no attachment to, or infiltration of, the adjacent structures.

Fig. 8.—Benign papillomatous cyst, showing the pedicle of the papilloma, with the fibrous tissue stroma and the covering of duct epithelium. The intracystic growth has in places the true papillomatous form, while in other areas there is a glandlike arrangement, the latter possibly due to a fusion of the papillae. In the tumor growth and in the surrounding tissue there is marked cellular infiltration and large quantities of blood pigment.

Microscopically the smooth wall of the cyst was lined with duct epithelium, occasionally flattened out, but usually columnar. Sections through the base of the papilloma showed the fibrous tissue framework, which contained the blood vessels, growing up from the connective tissue

about the cyst, and over this a covering of from one to several layers of epithelial cells, but usually a single layer of columnar epithelium (fig. 7). Often one could see clearly the delicately branching papilloma with the connective tissue covered with epithelium (fig. 8), while another common picture was a glandlike arrangement, with spaces lined with epithelium lying in the connective tissue (figs. 7 and 8). In still other areas the surface of the papilloma was covered with several layers of

Fig. 9.—Higher magnification of a papillomatous growth, with some hemorrhage between the papillae. There are many points of attachment of the growth, and at times it is difficult to follow the rather indefinite wall. Frequently, with the microscope one may become lost within this maze of growth, whereas with the dissecting lens or on gross examination a definite wall can be seen.

epithelial cells, or with these growing to form solid masses almost free from connective tissue. About the cysts were noted various grades and kinds of epithelial proliferation or inflammatory reaction, small cysts with papillomas, solid duct adenomas (fig. 9), nonencapsulated adenomatous areas (fig. 10), cystic adenomas, or dilated ducts. Around these could

be seen varying degrees of round or polymorphonuclear cell infiltration (figs. 7 and 11). Also, quite frequently the tissues were deeply stained from old hemorrhage, with enormous numbers of phagocytic cells loaded down with blood pigment (fig. 12). Associated with the foregoing conditions was every grade of fibrous tissue proliferation (figs. 12 and 13).

Fig. 10.—Section taken from a breast the seat of benign papillomatous cysts, showing a duct filled with epithelial cells and with the outline quite indefinite at places. About this duct are epithelial elements which are numerous for a breast that has never lactated, and all of these are located in an area of chronic inflammatory reaction and fibrous tissue proliferation. Areas like this, particularly in the frozen section, are often difficult to differentiate from cancer. This patient has remained well for five years since operation, at which time this type of tissue was cut through in removing the papillomatous cyst.

The multiplicity of these small areas and the distortion due to the hemorrhage and inflammatory reaction, together with their close relation to the wall of the large cyst, suggested occasionally that invasion

had taken place. Even microscopically at times the outline was not absolutely definite (figs. 8, 9 and 13).

A still more confusing picture was seen in a small percentage of cases that showed an area of hard, fibrous tissue, which grossly resembled scirrhous carcinoma, and which, microscopically, was found to be made up of dense, connective tissue or scar, scattered through which were

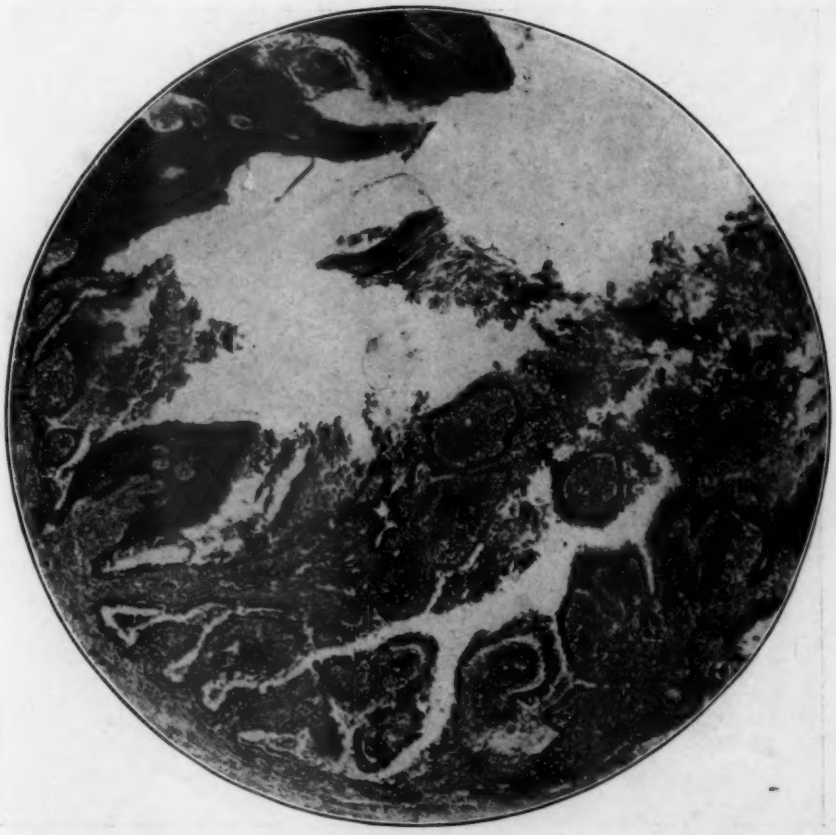

Fig. 11.—Extensive epithelial hyperplasia in a breast that had never lactated from the same patient as figure 9. This tissue was cut through at operation, and there was no subsequent tumor formation.

clumps of epithelial cells (fig. 13). On superficial inspection this had a structure similar to that of scirrhous carcinoma. However, on more careful examination the individual cells did not appear malignant, but were of uniform size, outline and staining reaction. No mitotic figures could be seen, and individually the cells suggested a benign, epithelial growth, probably breast acini and ducts that had been trapped or included in the scar tissue proliferation. So far as can be determined, we have no

record of a case which showed this picture alone and in which there was a recurrence, regardless of the type of operation performed.

The lymph glands were negative in the thirty-four cases noted, there being no record of involvement in any one of this series.

As to infection, every grade of inflammatory reaction has been encountered from a slight cellular infiltration to a cyst filled with cloudy

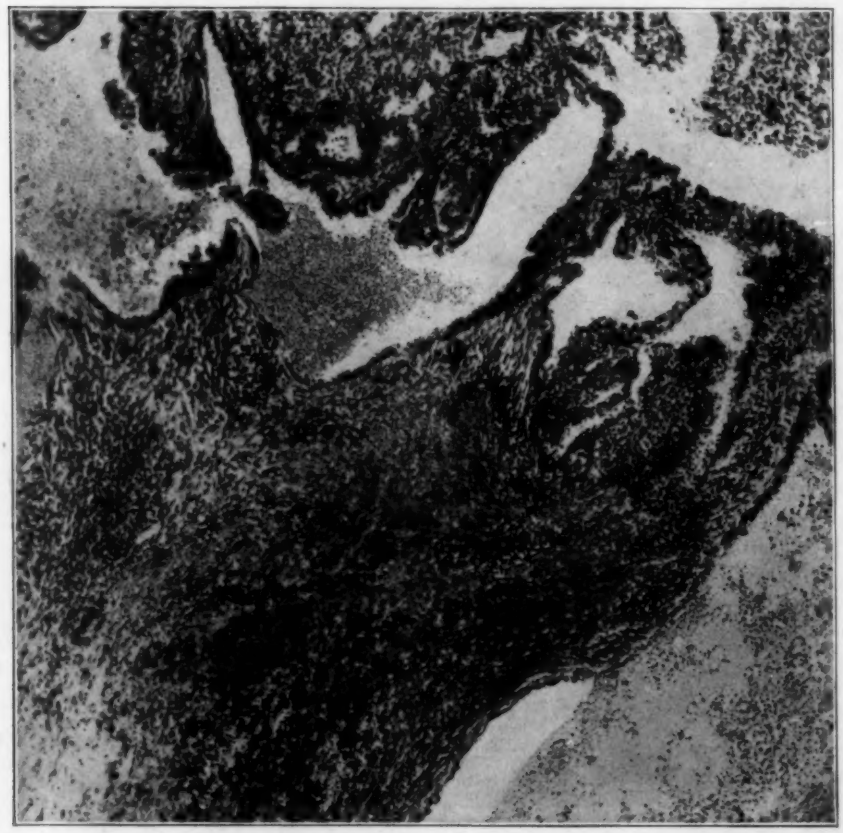

Fig. 12.—Papillomas arising from a duct within the nipple: on one side is the stratified squamous epithelium, with the sharp line of demarcation between it and the duct epithelium; the former is in close apposition to the papillomatous growth; there is marked inflammatory reaction as evidence of infection.

or purulent material, the papilloma having been largely destroyed and the surrounding breast riddled with minute abscesses. In the cases with the more severe grades of infection only a small, cellular, friable thickening of the wall had persisted to denote the location of the papilloma, and grossly this has often been called cancer. The misinterpretation seems to have been due to the adherence of the surrounding tissues, and the

extension of the inflammatory reaction into them, a condition quite evident in the microscopic sections. These are the cases which clinically gave the picture of cancer, and in which at exploratory incision it was impossible to rule out malignancy owing to the induration and fibrous tissue reaction which prevented an intelligent selection of areas for examination, since everything was suggestive. With this clinical picture the radical operation has been, and probably will continue to be, performed. The pathologist, however, with sufficient time to study many

Fig. 13.—Hemorrhage into the cyst and adjacent tissue: about the cyst are numerous phagocytic cells filled with old blood pigment; they are located in a scar due to the marked proliferation of connective tissue cells.

sections can make a diagnosis of a benign tumor, so that the patient can be reassured as to the outlook.

MALIGNANT GROUP: COMPOSITE PICTURE

The study of this group is based on twenty-four cases.

The malignant cases have shown clinically, grossly and microscopically characteristic and well defined carcinomas (figs. 14, 15, 16 and 17). Of the twenty-four cases, twenty-one were diagnosed clinically as malignant, two as doubtful, and one as benign. The latter three

Fig. 14.—Area which on gross examination was thought to be scirrhous carcinoma: there is a dense fibrous tissue formation and embedded within it are certain more or less normal epithelial structures; on one edge is a small tag of a papilloma. This picture, particularly in frozen sections, is easily confused with scirrhous carcinoma, and suggests an invasion of the structures about the cyst.

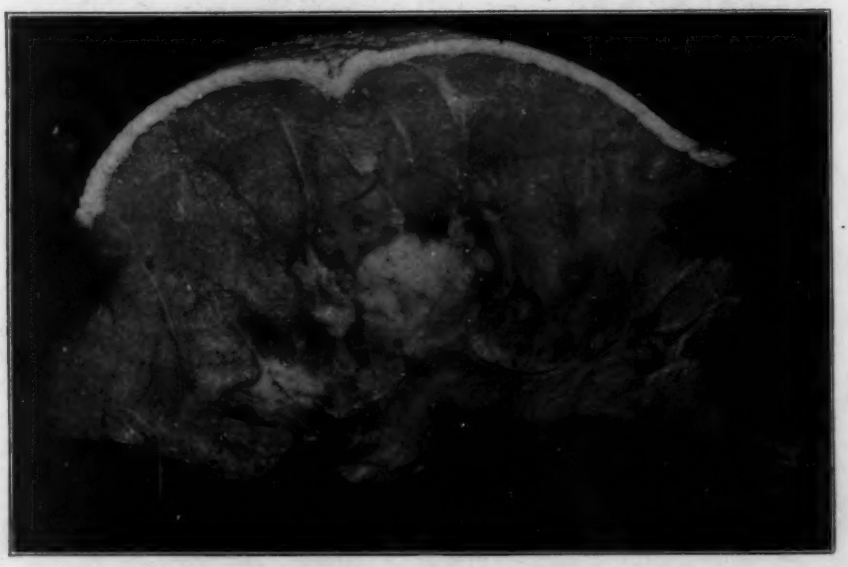

Fig. 15.—Scirrhous carcinoma in a breast the seat of multiple papillomatous cysts: the definite walls to the benign cysts as contrasted with the invasive nature of the malignant growth should be noted.

were diagnosed pathologically as cancer, and in the last, despite this diagnosis, the axillary dissection was not made until nine months later when the lymph glands were found replaced by a large, carcinomatous mass.

The age of onset in the malignant cases is shown in fig. 1 to lie between 35 and 71, but it should be noted that in one of the cases classed as suggestive of malignancy the patient was 27 years old. In

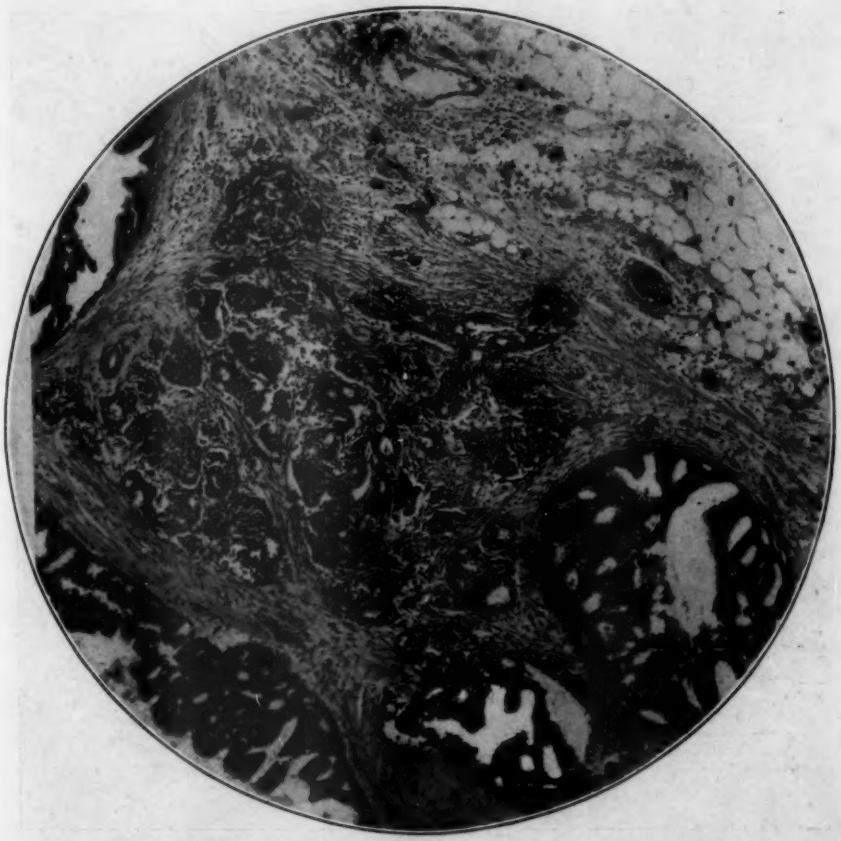

Fig. 16.—Medullary carcinoma located in a breast the seat of multiple small papillomatous cysts: the retracted nipple, thickened edematous skin, with a pigskin appearance, the soft cellular growth, with invasive properties and the numerous, small, blood cysts should be noted.

the predominance of cases the age is between 40 and 60, with the mean at 51.

The symptoms of onset were a lump in nineteen cases, nipple discharge in three and pain in two.

From figs. 3 and 4 it can be seen that most of the cases were of less than three years' duration, and in all except one the tumor had been

present less than six years. This last patient gave a history of a slow growth over a period of eleven years. The mass was then incised, only bloody fluid being obtained, after which the classical picture of malignancy rapidly developed. Evidently the tumor had been benign for a considerable time. This patient on clinical examination, thirteen years after onset and two years after the incision, had unquestionably a carcinoma, and the radical amputation was performed. She returned

Fig. 17.—Section of breast with extensive carcinoma, which is lying in close approximation to benign, intracystic papillomas.

two years after operation with an ulcerated, local recurrence and this within a year caused her death. Figure 2 shows that in the cancer group there has been a gradual increase in the average duration of the growth for each decade since 1890. This is contrary to what would be expected in view of the extensive, recent educational propaganda. On closer study, however, it is seen that this rise is dependent on two cases (six and thirteen years' duration), one in each of the last two decades, and that

if these are eliminated there is a gradual fall as is shown by the dotted line. The results of educating the public is better illustrated by the curve for the benign group. This consists of a much larger number of cases, and in consequence the data gained therefrom are more apt to be correct.

Nipple discharge was not such a frequent occurrence as with the benign group, occurring in only eight of the twenty-four cases, whereas a tumor was palpable in all (fig. 4).

In 60 per cent of the cases the tumor was 6 cm. or more in diameter, in the majority considerably larger, a condition which we would not expect to find at the present time.

In 65 per cent it was likewise noted as being hard, or "hard, like cancer." The nipple was retracted or showed fixation in fourteen out of the twenty cases noted. Skin changes were present in 75 per cent of the cases, and in 75 per cent there were enlarged axillary glands, two-thirds of which were clinically malignant on palpation.

Pathologic Examination.—This group showed predominantly single tumors, the majority having areas in the wall suggestive of cancer, with sixteen cases noted as "invaded" or with cancer in the wall, four as having thick walls, and with only one as not invaded. In this last case there were no metastases to the glands, and the gross description would suggest a benign tumor. It was described as a large cyst, with papillomatous projections, but with no invasion beyond the cyst wall. There was no local recurrence after radical removal, but five years later the patient came back with medullary carcinoma of the other breast, and with involvement of all the corresponding axillary glands. Her death was caused by metastatic carcinoma two years after the radical removal of this breast. From the sections which we have from this patient we have to call the first tumor cancer, though it is possible that these were taken from the intracystic growth, that the tumor of the other breast was a new development, and that this patient was cured of the first tumor. Of the cases with notes 55 per cent showed metastases to the axillary glands.

In all these cases except the one cited above, definite and well marked cancer with invasion was apparent (figs. 14, 15, 16 and 17), a picture that is not confusing in any way. A study of the sections shows that the cells very markedly in size, outline and staining reaction, that mitotic figures are abundant, and that the picture is that of typical cancer. It is entirely different from the pictures noted under the benign group, about which pathologists will disagree on a considerable number of cases. However, in these same breasts one very often sees some picture that was noted above under the group of benign papillomatous cysts, and these may, or may not, be in intimate association with the cancer (figs. 14, 15, 16 and 17).

DOUBTFUL GROUP: BENIGN OR MALIGNANT

A composite picture of this group is not given, since their character is a matter of uncertainty, and accordingly each case is given in detail under the report of cases. In reading over the records, I find nothing in any of the histories or examinations which could not well go with the benign group. Even the pathologic reports of "medullary carcinoma," "adenocarcinoma" and "typical adenocarcinoma of the papillary type" can be duplicated several times in the early diagnoses of cases now thought to be unquestionably benign. The case diagnosed as cancer without microscopic confirmation must unquestionably be placed as doubtful.

My own feeling is that all of these cases were benign, and were they added to the benign group they would cause little change in that composite picture other than an increase in the number of patients submitted to radical treatment, as well as in the number cured.

Two patients are dead, one after three and one-half and the other after eight years, of causes other than cancer. Three patients are living and free from recurrence, two, four and thirteen years after operation. The removal of these, together with the many benign cases, from the malignant group, has so reduced the number of cases of cured cancer that in the remainder a poor prognosis must be given instead of the usual encouraging report based on their "relatively low grade of malignancy."

ULTIMATE RESULTS

Benign Group.—Of the sixty-six out of ninety-five patients in this group who could be followed, not one showed any evidence of recurrence. Nine are dead: one after one year, by suicide; one, after one year, of carcinoma of the cervix; one after two years, in an automobile accident; one after three years, of pulmonary tuberculosis; one after seven and one after eight years, both probably of cerebral hemorrhage. In addition, three who did not have any recurrence are said to be dead.

Malignant Group.—1. Of the ten patients in this group who showed metastases to the glands, one has recently died of recurrence three years after operation; six died of recurrence and metastases within five years; one died of some unknown cause one year after operation; two died of "pneumonia" and "heart trouble" after ten and twelve years, respectively.

2. Of the nine patients without lymph gland metastases: for one there is no note; one died of streptococcal wound infection on the second day after operation; two died of metastases within one year after operation; one died of medullary carcinoma of the other breast (noted above with question as to malignancy) after seven years; one died after four years, without recurrence (morphine addict); one died of pneumonia, after six years, having had no recurrence; one died of some unknown cause six years after, and one is well seven years after, operation.

3. Of the four patients with no note on the glands: two died of metastases one year after operation; one had had no recurrence after ten years and died of some unknown cause thirteen years after operation, and the other patient could not be followed.

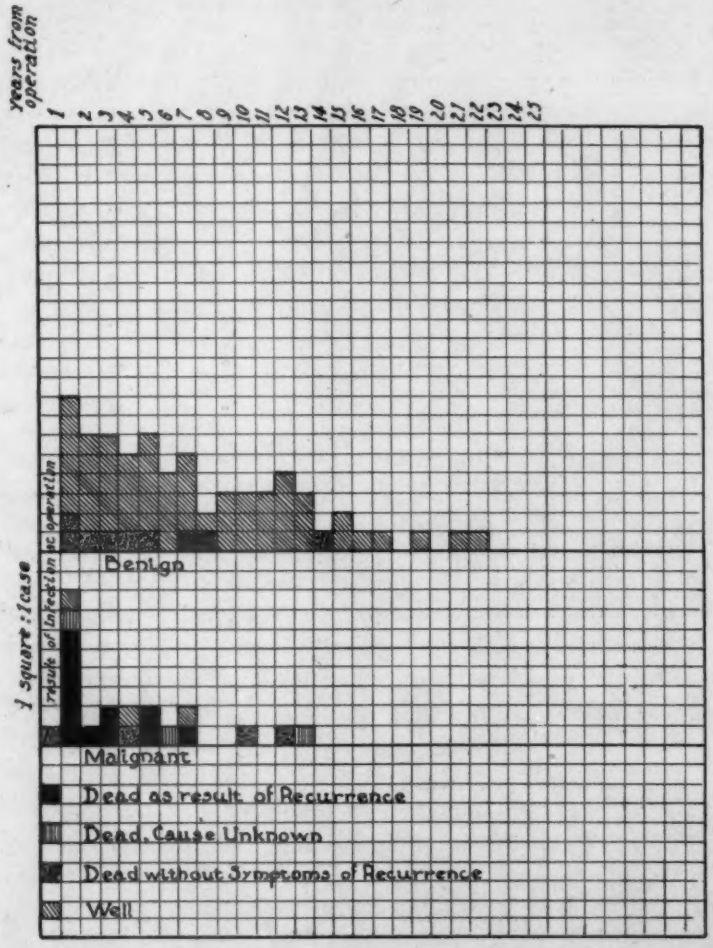
Years from operation
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
1 square: 1 case
Benign
Malignant
Dead as result of Recurrence
Dead, Cause Unknown
Dead without Symptoms of Recurrence
Well

Fig. 18.—Carcinoma, papillomatous cysts and intracanalicular fibro-adenoma located in the same breast and in such proximity that all can be seen under one field of the microscope.

Doubtful Group.—No patients died of cancer or showed evidence of recurrence.

From this and from figure 18 it can be seen that among the benign cases there is no evidence of any patient having had a recurrence, while of the malignant group: twelve patients have died of recurrence, three of other causes and two of some cause not stated, during the period of

Summary of Cases

History	Benign (95 + 9 bilateral operations = 104 cases)		Malignant (24 cases)	
	Number	Per Cent	Number	Per Cent
Clinical Diagnosis:				
Benign	61	64	1	4
Malignant (clinical or exploratory)	34	36	21	95
Symptom of Onset:				
Nipple discharge	47	48	3	12.5
Tumor	37	38	19	79
Pain	13	13	2	8
Summation of Symptoms (104 cases benign; 24 malignant)				
Nipple discharge	69	66	8	33
Tumor	85	81	24	100
Pain	43	41	16	67
Clinical Examination:				
Number single	62	83	18	85
Number multiple	13	17	3	15
Size:				
1 to 2 cm.	25	43	2	10
3 to 5 cm.	11	19	4	20
6 cm. +	22	38	14	70
Consistancy:				
Soft, fluctuating, cystic	29	37	3	15
Tense	2	2.5	1	5
Encapsulated, circumscribed	5	6	..	..
Firm, nodular, shotty	33	42	..	..
Indurated	7	9	..	..
Hard, hard like cancer	2	2	16	80
Nipple:				
Normal	43	65	8	40
Slightly retracted	12	18	0	..
Protruded	3	5	0	..
Retracted	8	13	12	60
Skin:				
Normal	49	71	4	17
Tense, red, ulcerated, sinus	9	13	4	17
Slight change	9	13	0	..
Dimpled	2	3	3	12
Infiltrated; attached; pig-skin; metastases	0	..	15	62
Dilated veins	0	..	2	8
Mobility:				
Movable	42	98	6	54
Attached	1	2	5	45
Lymph Glands:				
Negative	64	86	5	25
Palpable	9	12	5	25
Hard, suggestive of cancer	1	1	10	50
Operation:				
Tumor	22	22	0	..
Breast	41	40	1	4
Complete for cancer	38	38	23	96
Pathologic Examination:				
Number single	51	63	20	91
Number multiple	30	37	2	9
Character:				
Cyst with papilloma	89	100	2	9
Cyst with papilloma and thick area in wall	0	..	4	18
Cyst with invasion or cancer in wall	0	..	16	73
Cyst Wall:				
Not infiltrated	50	96	1	7
Thick	2	4	1	7
Infiltrated	0	..	13	87
Cyst Fluid:				
Bloody	60	83	9	82
Clear	8	11	0	..
Other type	4	6	2	18
Lymph Glands:				
No glands removed	57	63	0	..
Negative	34	37	9	45
Metastases	0	..	11	55
Ultimate Result:				
Number of cases followed (95 benign and 24 malignant)	66	70	22	92
Living and well, 1 to 22 years	57	87	3	13
Dead, no recurrence, 1 to 14 years	9	13	4	18
Dead, cause unknown, 1 to 13 years	0	..	3	13
Dead from cancer, 1 to 7 years	0	..	12	55

probable recurrence; three patients lived ten, twelve and thirteen years, respectively, while three patients are living and well one, four and seven years after operation.

EXPLANATION OF TABLE

The accompanying table covers the entire data in this article. Under both the benign and the malignant group is given in one column the number of cases, and in the other the percentages; the latter, according to the suggestion of Dr. Raymond Pearl, are based on the actual number of cases for which we have a definite note. This in general causes the percentages to be based on a summation of the figures in the first column for each major division. An exception to this is for the summation of the symptoms of tumor, nipple discharge and pain, in which the symptoms overlap, and the percentage is necessarily based on the total number of cases, since all the patients complained of one or more of these symptoms.

COMMENT

From our own records and from the literature it is evident that cases belonging to the benign group of these tumors have been most frequently misinterpreted and as a result a large percentage of the patients have been subjected to an operation more extensive than is justifiable except for malignancy. In the majority of cases this has followed either the excision of the tumor or an exploratory incision, since the lesions were clinically benign or only suggestive of malignancy. The more radical operative procedure has been based on the finding of a cyst filled with bloody fluid, and with a soft, friable, papillomatous tumor attached to the wall. Without further thought the surgeon has closed the wound and performed the radical operation or, being in doubt, has been content with that unjustifiable, halfway procedure of removal of the breast alone. The latter operation is evidently not radical enough for cancer but is too extensive for a benign lesion, save in the occasional case in which one or multiple tumors almost replace the breast.

There was one group of patients who gave the clinical picture of malignancy and who were submitted to the radical operation without exploration. This included a large part of the cancer group, and also those cases showing the more severe grades of infection. These benign tumors associated with extensive infection were the only ones of the simple papillomatous cysts that were clinically malignant. Since it was almost impossible to rule out cancer in these cases in which the breast contained large, cystic tumors associated with the superimposed infection that had produced an induration, thickening of the wall and adherence to the surrounding tissues, they had to be treated as cancer.

We will dismiss as having received proper treatment this group of clinically malignant cases in which no mistaken diagnoses have been found, except for the occasional infected cyst that has been called cancer. There remain that larger number of cases that we consider to be clinically benign. In these there were frequently slight changes in the nipple, skin or lymph glands which were suggestive of malignancy, or the tumor itself was unusually firm or irregular for a benign lesion. These conditions are considered below, and explanations as to their causation are offered which, if accepted, make it evident that such slight changes have to be discounted in this type of tumor. A careful analysis of the mistaken diagnoses in this series shows that the clinical impression of malignancy has been founded on the bloody discharge and on the slight changes in the skin, nipple and axillary glands, together with the consistency of the tumor. Or, more frequently, the deciding factor has been the gross or microscopic examination at the time of exploration. Surgeons have come to look on blood in a cyst as evidence of cancer, but the foregoing data seem sufficient to justify us in ignoring the cyst contents and in emphasizing the importance of a careful study of the attachment of the wall to the surrounding structures. We are justified in treating the tumor as benign if the wall is freely movable over the adjacent tissue and there is no evidence of invasion.

In addition to the explanations of these observations which are offered below, we shall compare or contrast the benign and malignant groups, as well as correlate the data obtained from this study with the reported cases, more particularly the larger series found in the literature.

Age.—Intracystic papillomatous tumors of the breast are usually considered to belong to middle or advanced age; Deaver and McFarland state that they usually occur in the breast of women who have passed the menopause, and give the average age in their cases as 46.6 years. In the cases reported by Warren the average age was 52; in those of Greenough and Simmons it was 49.5, while in the compiled cases of Williams it was 43. In this series the mean age was 42, with sixty of the cases in patients less than 45, while eight occurred in women less than 25 years of age (fig 1).

In the cancer group all our patients were more than 35 years of age. However, in the doubtful group there was one patient younger—only 27. This, together with the fact that cancer of the breast occurring before 25 years of age is a most unusual condition, would justify treating a definite number of these cases as benign, unless they are unquestionably malignant. Despite the age of the patients, however, in some the diagnosis of cancer has been made and they have been submitted to radical treatment. The most striking case occurred in a girl whose first trouble —a bloody discharge from the left nipple—came on at the age of 15.

three years after the onset of menstruation. This ceased after a short time and a lump appeared, which gradually increased in size and was painful. We have no record as to the size the tumor reached, but the sections show extensive epithelial hyperplasia throughout the gland. Only the breast was removed, one year after onset, the patient being then 16 years of age. In 1923 the patient, then 17, returned with a bloody discharge from the right breast and some little nodules in the skin of the left chest. The right breast was removed in June, and three weeks later the tissues about the scar on the left chest and the left axillary glands. This last operation was performed because of the gross diagnosis of cancer and a microscopic report of papillary adenocarcinoma of the breast. The lymph glands were not implicated and unfortunately the skin nodules were lost, so that their character could not be determined. The case was diagnosed by us as multiple, benign, papillomatous cysts, and by Ewing as papillary cystadenoma. We feel that the extensiveness of the condition demanded removal of the breasts, but that the radical removal of the tissues from the left chest wall and the axillary dissection were not indicated. The burden of proof would certainly rest on the person who makes a diagnosis of cancer of the breast in a person of this age.

Variation in Size of the Tumor.—Mention is made in the literature of the variation in size. Bowlby [12] reported a case of spontaneous cure, which we interpret as meaning that the tumor disappeared. Williams [1] mentions a tumor which suddenly appeared beneath the nipple with a cessation of the discharge. This case is also cited by Deaver and McFarland. Greenough and Simmons [6] state that in some cases pressure caused a discharge from the nipple with a decrease in size and softening of the consistency of the lump. Such a discharge is of fairly frequent occurrence, and, when this history can be obtained, is suggestive of a cyst. Decrease in size associated with a nipple discharge and enlargement of the tumor when the discharge ceases means that we have a cyst connected with a duct. This condition is most frequently seen in the papillomatous cysts, and if the discharge is bloody, it is almost pathognomonic. A recent exception to this was a case of colloid carcinoma that involved the entire breast, with a breaking down and destruction of all the tissue up to the nipple.

Discharge from the Nipple.—The discharge needs no explanation when the cyst is formed by a dilatation of the ducts, and here, as with papillomas elsewhere, bleeding is the rule. The type of discharge sometimes varies from clear or amber to bloody, probably dependent on trauma to the tumor. Here it should be urged that a bloody discharge from the nipple, with no other clinical conditions, should demand close observation, but should not be considered an indication for operation.

12. Bowlby, A. A.: St. Bartholomew's Hosp. Rep. **24**:263-272, 1888.

Ten of our patients were operated on for this alone and grossly or microscopically there were one or more small cysts with papillomas. Quite a few of this series have shown, after operation, a bloody discharge from the nipple of the same or opposite breast, but have had no further treatment, and none have developed cancer.

Bloodgood [13] in working up the significance of a bloody nipple discharge found cancer in about 1 per cent of cases. Furthermore, I think it will be generally conceded that the discharge in the majority of cases is dependent on the presence of a papillomatous cyst. This is one argument against the acceptance of a bloody discharge alone as indicative of malignancy. Other strong arguments are the observations in this group of cases, namely: (1) that 48 per cent of the benign and only 12 per cent of the cancer cases have a nipple discharge, which usually is bloody, as the symptom of onset; (2) that 66 per cent of the benign cases, as contrasted with 33 per cent of the cancer cases, at some time showed this nipple discharge; (3) no case of cancer showed nipple discharge unless tumor was palpable. A bloody nipple discharge, however, is held by Delbet and Mintz (cited by Ewing) as a sign of probable malignant degeneration.

One interesting section that recently came under our observation was from shreds given off with the bloody discharge, and showed the typical papillomatous arrangement. A diagnosis of a papillomatous cyst was made, but as it is not known whether or not this patient has had an operation since that time, the case is not included in this series.

Pain.—It is pain that brings the patient earliest for operation, this having a much shorter duration as a symptom than the tumor or nipple discharge (fig. 4). This is all the more striking when one considers that it is such a variable condition, frequently present only when there is a cessation of the discharge, and usually is not severe. It was present in one half of Greenough and Simmons' cases and in one third of the compiled cases of Deaver and McFarland, and was never severe. In other reports it is stated that pain is quite rare. In our cases there is a higher percentage of pain in the malignant group, in 67 per cent, as contrasted with 41 per cent in the benign group.

Location.—It can be assumed, as in the literature, that these tumors lie in dilated ducts, or that the cysts arise from dilation of the ducts, since a large percentage of them have direct connection with the surface through the duct opening at the nipple. Furthermore, in one of our cases and in one of those of Greenough and Simmons, a microscopic section shows the duct continuous from the cyst to the surface of the nipple. On microscopic study these cysts are frequently lined with columnar duct epithelium (fig. 7), so that it can be readily understood that they are predominantly tumors of the central part of the breast. In several

13. Bloodgood, J. C.: Surg. Gynec. Obst. **3**:721, 1906.

cases reported in the literature the papilloma has projected from the nipple and has reappeared when cut off or cauterized. We have one section through a duct just at the nipple showing stratified squamous epithelium on one side and the papilloma arising from the adjacent duct epithelium (fig. 11), while in another case the growth was located entirely within the nipple.

Multiple Tumors.—From the accompanying table it is seen that these tumors are frequently multiple, particularly on pathologic examination. But if there were added to this table all the cases which showed in microscopic section the small papillomatous cysts about the larger tumor, the nine patients who at a later time underwent an operation for a similar tumor and the half dozen or more patients who had a subsequent bloody nipple discharge, almost undoubtedly due to a similar small papillomatous cyst, it would be evident that this is definitely a condition with a tendency to multiple separate tumors. This is well illustrated by the followng cases.

REPORT OF CASES

CASE 1.—*History.*—C. F. M., a woman, aged 34, a few days before admission noted a bloody discharge from the left nipple, and her physician found two lumps. Examination in the Johns Hopkins Hospital dispensary showed two lumps in the left and one in the right breast, all freely movable, not adherent, encapsulated, nonfluctuant and located near the nipple.

Gross Pathologic Examination.—Nodules ruptured during removal, with discharge of a chocolate colored, cellular material, said to be "suspicious of malignancy." Accordingly, the lower, outer quadrant of the left breast, including the tumor area, was excised. (No note was made on the treatment of the tumor of the right breast.) Numerous cystlike nodules varying in size from a pinhead to 1 cm. in diameter could be felt; not all of these were removed. On section they were found to contain a chocolate colored fluid and cellular detritus similar to that found in the larger nodules.

Microscopic examination showed multiple intracystic papillomas.

The patient has been well since the operation in 1915.

CASE 2.—This patient is a physician and has kept a close observation on her breasts since onset. Our records show the following:

1909. Bloody discharge from the right nipple; no tumor. Patient placed under observation, but no operation.

April 23, 1913. Excision of a benign papillomatous cyst from the right breast was performed. The discharge had ceased about six months before, and following this the lump had appeared. Microscopic examination of the tumor showed the papilloma with a fine connective tissue stroma and a definite wall about the cyst. Outside the larger cyst there were other small papillomatous cysts, and lobules of breast tissue showing mastitis.

Jan. 24, 1914. The patient reported that there had recently been a palpable tumor in the left breast, but this had disappeared after being present for a few weeks.

April, 1917. Three months previously there had been a bloody discharge from the right nipple lasting a few weeks. Examination showed that both breasts were symmetrical and soft, the right breast showing the scar from the previous opera-

tion. There was no suggestion of a tumor either in the right breast from which there had been recent bloody discharge, or in the left breast in which a tumor had been present for a few weeks in 1914, and had disappeared.

Oct. 8, 1924. The patient wrote as follows: "There has been a bloody discharge from the right nipple since the first of the year, but without a palpable tumor. On five or six occasions there has been a dull pain through the breast, but at these times I have realized that the discharge had been obstructed by a bit of cotton adhering to the opening. If I express the discharge it becomes bloody after the first few drops." She felt that there was no urgency at that time, since, if the cyst kept discharging, it would cause no harm except to her clothes, but that in case the discharge should cease while there was inflammation in the ducts a cyst would form, and have to be cut out. She cited her previous experience as justification for this opinion.

With only the palpable tumor and the adjacent breast tissue removed, one must expect that similar tumors or a bloody discharge will develop in a certain number of cases. In our series, even with the entire breast removed in 78 per cent of the cases, 15 per cent of the patients had further tumors or nipple discharge on the same or opposite side.

This is contrary to Ewing's opinion that the tumors are usually single, occasionally multiple, and rarely bilateral. Deaver and McFarland also state that they are almost invariably single, but go on to describe them as irregular in outline and having a consistency varying in different areas. This we have found to be due to multiple, small, closely located tumors. Bowlby and Morton (cited by Deaver and McFarland) each give a case of recurrence. Greenough and Simmons have two cases recurring (six and eighteen months) after operation. It seems to us that these "recurrences" have more probably been the result of the growth of other small tumors which had been left behind. In the 15 per cent of our benign cases in which there was further trouble, the second tumor has not necessarily or usually been in the scar from the excision of the first tumor; frequently it has been in the opposite breast.

Nipple Change.—The changes in the nipple in the benign group—in the twelve cases with slight retraction and in some of the eight cases with more marked retraction—can be easily explained by the location of the tumor. The nipple changes have to be discounted with tumors located, as these are, beneath the areola, since the mechanical pressure on the ducts with the resultant displacement causes a tugging on the points of their attachment. Since they converge to the nipple where they are attached and this part of the breast is quite mobile, it is drawn in according to the amount of shortening caused by the displacement of the middle portion of the ducts. Furthermore, if the tumor involves the duct itself, this pull is the more easily understood. In a recent case with a single, superficial cyst, without a papillomatous tumor, in each breast near the nipple one could slide either of the freely movable tumors along beneath the skin and cause a complete inversion of the correspond-

ing nipple. At operation these tumors were found to be cystic and connected to the nipple by a definite cord, suggesting a duct, but no fluid could be expressed. It is evident that if in these cases one tests the nipples by lifting them, there may readily be found a certain amount of fixation. Some of the patients with retraction showed infection, and one had had the nipple retracted since the birth of her first child, sixteen years before. In two cases with the nipple obliterated, in addition to the tumor there was a marked inflammatory reaction.

According to Deaver and McFarland, the nipple is never inverted in uncomplicated cases. They cite, however, a case with the growth beneath, and with part of the papilloma projecting from the nipple and causing inversion. Ewing states that the nipple may be retracted.

Consistency.—The malignant group showed in general the consistency of cancer. Of the seven cases in our benign group in which the tumor was noted as indurated, four showed infection. The three remaining, together with the thirty-three noted as firm, nodular or shotty, can be easily explained by anyone who has felt a tense cyst in the breast, if he but imagine this surrounded by multiple small tumors of a similar character, which are usually found on pathologic examination. The two cases noted as "hard, like cancer" both showed infection. Greenough and Simmons state that they are hard if tensely filled with fluid. Deaver and McFarland state that they are generally irregular, lobular or lumpy, the majority giving the impression of solid tumors.

Mobility.—Only one of the benign group showed attachment and in this case there had been an extensive infection, and the mass had ruptured before the patient came under observation. In about half the malignant group in which a note was made on mobility, the tumors were attached. Where noted in the literature these tumors, whether diagnosed as benign or malignant, were freely movable except in occasional cases, which from the history and findings suggest cancer.

Lymph Glands.—The lymph glands were essentially negative in the benign group except in one case with marked infection, in which the glands are recorded as "hard, like cancer." Despite the clinical diagnosis of malignancy, on account of the age and feebleness of the patient, only the breast was removed. The existence of a benign papillomatous cyst with infection is now generally recognized. Unfortunately, we have been unable to trace this patient, she having been treated in the early days of the hospital. In nine cases the glands are recorded as palpable, but frequently with the note that they are not hard, like cancer, and wherever the glands were studied pathologically they showed no metastases. When one considers the number of these cases with infection, it is surprising that not more of these patients had enlargement of the axillary lymph glands. On the other hand, 50 per cent of the malignant

group were diagnosed as having metastases into the adjacent lymph nodes, and on pathologic examination it was found that in 55 per cent of all cases the axillary glands were grossly and microscopically involved.

This high percentage of lymph gland involvement tends to strengthen our impression that many of the tumors heretofore reported as cancer are benign, since it is a strongly established opinion that the lymph nodes are involved only late in this type of so-called malignancy. Very few of the cases reported as cancer have shown it. Ewing states that the lymph nodes have a prolonged immunity. Bloodgood's report [14] in Gynecology and Abdominal Surgery by Kelly and Noble is based on eighteen benign and fourteen malignant cases. Five out of six of the latter patients remained well. Only one of these had lymph gland involvement, and in several of the cases the diagnosis has since been changed to benign.

Infection.—We find infection to be fairly common, but it is not mentioned in the literature of these cases so far as we have been able to determine. It has been clearly shown in the foregoing that infection can give the clinical picture of malignancy and these breasts will have to be sacrificed. For anyone who has tried to keep a draining sinus sterile, it is easy to understand the possibility of a high percentage of infection in these cysts. They are filled with a good culture medium, frequently there is a large dead space, with intermittent or slow discharge, and practically no attempt at asepsis. Fortunately, in most cases it is a very low grade affair, with a chronic inflammatory reaction, showing on microscopic examination, round-cell infiltration, with a few scattered polymorphonuclear cells. However, four of these cysts had ruptured, one on three occasions, and three patients came in with a draining sinus through the skin away from the nipple. Another case, diagnosed as abscess, showed all the signs and symptoms of acute inflammation, and the papillomas were discovered only on pathologic examination. One of these patients had intermittent attacks of conjunctivitis, and the organism, an unclassified bacillus grown from the nipple discharge, was found to be identical with what was apparently the etiologic agent in the eye condition.

Here it should be noted that we have no record of a patient with cancer coming in with a draining sinus. In the early cases a fairly large number showed ulceration and even now an occasional patient comes in with this condition. Of course one of these cysts, with an associated cancer or possible malignant degeneration, would be liable to develop a sinus from the rupture of the cyst, but we have not met with such an instance.

Pathologic Observations.—Associated with these tumors there is often an extensive epithelial hyperplasia which may assume one or more

14. Bloodgood, J. C., cited by Kelly and Noble in Gynecology and Abdominal Surgery, Philadelphia, W. B. Saunders Company, 1908, vol. 2, p. 194.

of several forms. It may be simply a part of the condition that causes the multiple papillomas. There are two pictures, however, for which it is interesting to attempt an explanation.

One is the glandlike arrangement of the papilloma in places (fig. 8), and seems to us to be due to the manner of cutting the sections, or dependent on the fact that the various papillae have become adherent and fused, with a loss of the epithelial cells at the point of fusion. Similar pictures are frequently seen in the fallopian tubes following an inflammatory lesion. The other is the hard area with a rough resemblance to scirrhous carcinoma (fig. 13). It seems that this could well be explained by the entanglement of certain epithelial elements and their inclusion in the formation of fibrous tissue, the latter reaction dependent on an irritation, either from the tumor and associated hemorrhage into the tissues, or from infection superimposed on the papillomatous cyst.

Probability of Malignant Change in the Benign Group.—These tumors have been looked on as especially liable to malignant degeneration, and, as for all breast tumors, their removal is demanded when there is a definitely palpable tumor. From figures 3 and 4 it can be seen that there are thirteen patients in the benign group who had had a tumor of from five to twenty-five years' duration and six with a nipple discharge extending over a similar period. Furthermore, one of our patients, aged 72, who had had a papillomatous cyst with a bloody discharge for one year, stated that her mother, then 96 years of age, had had a cystic tumor for many years, with onset soon after the menopause, associated with a continuous discharge from the nipple, the character of which had varied between bloody and serous. Her mother's health was good. There also were several cases cited in the literature with a duration of from ten to thirty years. On the other hand, we have one patient who gave a history of thirteen years' duration, with slow growth to the size of a walnut at the end of eleven years. At this time it was cut into, without an anesthetic; only bloody fluid was obtained, and no further treatment was carried out. There was no history of nipple discharge. After that time it had grown rapidly, increasing 300 per cent in size within two years, and a prickling pain had been present for three weeks before admission. Examination showed a tumor in the outer half of the breast, attached to the old scar, and below this a large cystic swelling. It was associated with enlarged axillary glands, and was diagnosed clinically as carcinoma with cystic degeneration. The radical operation was performed and the specimen showed, grossly and microscoically, cancer in the mammary gland and axillary lymph nodes. In the breast it was intimately connected with a cyst which was filled with bloody fluid and in which there was a projecting papilloma. The patient died recently from an extensive recurrence. This is the only malig-

nant case we have of more than from five to six years' duration, and with a history suggestive of a cancer developing in a benign tumor. However, this is not such a high percentage of malignant change as one is led to expect from a study of the literature. Certain facts strongly suggest that the malignant cases, with the exception of the one referred to, were cancer from the onset. These facts are: (1) In fifteen of the twenty-one cases of cancer in which the duration is known, the patients came to operation within two years of the onset (fig. 3); (2) in only two cases was there a history of more than five years' duration (six and thirteen years, the latter case previously noted), and (3) in only 38 per cent of the benign group, with an average duration of 3.3 years, the tumors were 6 cm. or more in diameter, while in 70 per cent of the cancer group they had reached this size after an average duration of only 2.5 years.

Comparison of the Impression Based on a Clinical Study with That Made at the Time of Actual Examination.—From a study of the records of these cases, we find that in the cancer group there have been relatively few mistakes clinically and none pathologically. If the cases with marked infection are removed from the benign group, none of them gave a definite picture of malignancy. Certain cases were noted as suggestive of malignancy, but in reading over the histories and physical examinations in view of this study, we find that the impression has been based on such things as slight changes in the nipple, the firm, lumpy or nodular character of the tumor, the bloody nipple discharge, and so forth, which must be discounted, as is here explained. With this in mind, the findings are almost entirely more those of a benign than of a malignant tumor. The mistakes in the majority of cases have been due to the exploratory incision; the surgeon, finding bloody fluid or a papilloma, has immediately closed the incision and performed the more radical operation. At the present time, owing to the fact that all superficial tumors come earlier under observation, and because of the greater difficulty in diagnosing cancer at this stage, it is imperative that every definite nodule in the breast should be removed. This, from the patient's standpoint, puts the ultimate diagnosis up to the surgeon at the time he removes the tumor. He should have the pathologic picture of this tumor in mind whenever he makes an exploratory operation.

Ultimate Results as Proof of the Correctness of This Division into Two Groups.—In conclusion, it seems that the ultimate results (fig. 18) offer sufficient proof that our division into these two groups is in the main correct. Our cancer group with 50 per cent of the patients dead as a result of recurrence or metastases, three dead from other causes during the period of probable recurrence, two dead during this period from causes not stated, and with only three patients living at the present time, one, four and seven years after operation, is in marked

contrast to the widespread impression that these are tumors of a relatively low grade of malignancy. It seems clear to us, however, that this impression has been founded on mistaken diagnoses in which many of the benign cases have been called cancer.

METHOD OF ATTACK AT OPERATION

Based on the foregoing study, the following method of attack is suggested as offering the best chance of proper treatment. If the tumor is definitely malignant clinically, the radical operation should be performed without an exploratory incision. If it is thought to be benign, or if there is only such suspicion of malignancy as to demand exploration, and the tumor is not of such a size as mechanically to demand the removal of the breast, it should be *excised* with a zone of surrounding tissue. It should be immediately sectioned and examined for malignancy. Here one should be familiar with all that is included under the pathologic examination and should examine for the thickness of the cyst wall, its character, mobility of the wall over the surrounding structure, and should note particularly the attachment of the papillomas to the adjacent structures.

From any suspicious areas, either of increased firmness, unusually firm attachment of the pedicle of the papilloma, or where there is a question of invasion of the surrounding structures, blocks should be taken and sections made immediately. These sections should show the base of the pedicle and the tissue from which the papilloma arises. One section taken at random by the operator without seeing the entire specimen, or by the pathologist, without a careful gross examination of all the tissue, is worse than useless. It may give a false impression of benignity; or, if from the papilloma, it may be diagnosed as cancer, when the tumor is encapsulated, lying in a cyst with thin, smooth, freely movable walls. In this connection we might cite a recent case, not of papillomatous cyst, in which the operator, on demand of the patient, explored a breast tumor that was clinically malignant; he came down on a definite nodule lying on the edge of an indurated area in the breast. This small tumor was excised from the surface of the larger mass, and the operation delayed for the frozen sections which showed a typical intracanalicular fibro-adenoma. (Figure 17 is a similar case in this series.) The operator accepting this diagnosis of a benign tumor, and thinking that the involved area was so large as to include most of the gland, amputated the breast alone. Pathologic examination a few minutes after the close of the operation showed on one side of the tumor mass an area measuring from about 1.5 to 2 cm. in diameter, which was considerably harder than the surrounding tumor and which had a gritty consistency. On running the finger across it, one could mark out one border as definitely as the edge of a wooden shelf; on the other side it shaded off into the sur-

rounding tissues. In short, this was a case of a very small primary cancer growth, associated with benign tumors, and with extensive invasion of the lymph channels of the breast. The axillary dissection was performed soon afterward; the sections showed early involvement of all the adjacent lymph glands, with the lymphatics along the small vessels in the axillary fat plugged with tumor cells. In this case the operator's first and clinical impression of cancer was entirely overruled by a pathologic report from the examination of a small nodule not intimately associated with the true and really important tumor. On the other hand, when a careful gross examination shows a thin wall to a papillomatous cyst, freely movable over the surrounding structures, with no evidence of invasion at the attachments of the pedicles (figs. 6 and 7), the condition may be treated as benign regardless of what report the pathologist may make from an examination of the papilloma alone.

If a diagnosis of malignancy is made at *exploratory excision*, the wound should be cauterized and the complete operation immediately performed. If there is any doubt, the patient should have the benefit of the radical operation.

There will be a small number of cases that will present the earmarks of malignancy, and in these the complete operation is indicated. Some of these will prove to be cancer, but others will show infection of a benign papillomatous cyst. In the latter group exploration is practically useless, since the picture is so distorted, both grossly and microscopically, that the operator would probably still be in doubt unless he relied on the report based on a study of sections made from a block taken at random—a report that would be worse than futile.

Here it should be urged that after any examination of a gross specimen, particularly in the case of the papillomatous cyst, aseptic precautions should always be preserved. Since the most important thing is the examination of the specimen for diagnosis, and since this responsibility lies on the operator, it would be better for him either to drop out and have the wound closed by an assistant, or else after the examination of the specimen to change his gown and gloves. This is imperative, both because a soft, friable papilloma could be easily transplanted, and also because these cysts, connected with the surface by a duct, with a constant or intermittent discharge of contents, are particularly prone to infection, which, if transferred to the wound, would cause a breaking down of the incision.

SUMMARY

Benign Group.—The benign papillomatous cyst is a distinct type of tumor, presenting a fairly uniform history and physical findings. A nipple discharge, usually bloody, occurred in 66 per cent of these cases. This tumor sometimes gives a nipple discharge without a palpable nodule.

This discharge alone demands close observation, but is not an indication for operation.

Age: Tumors of the benign group in our series have appeared at any age after puberty; the malignant only after 35 years of age (one case suggestive of malignancy in a patient of 27).

Sex: They are rarely found in the male breast (2 per cent).

Duration: They may be of any duration; some in this series were present for from twenty to thirty years.

Consistency: They may have a firm, nodular and indurated consistency, due to multiple cysts, tensely filled with fluid and so situated as to suggest a single tumor.

Location: They occur predominantly in the central zone of the breast, but occasionally in the periphery.

Number: Clinically, they occurred as a single tumor in 83 per cent of the cases but other tumors developed later in 15 per cent. The specimens showed other tumors, on pathologic examination, in about 50 per cent of the cases.

Size: They usually are small, but they were over 6 cm. in diameter in 38 per cent of the cases.

Nipple: There may be some retraction of the nipple due either to the mechanical action of the tumor in pressing on the ducts, or to the contraction of scar tissue where infection is superimposed.

Skin: The skin usually is normal, but may be tense, thin, shiny, red, or show a sinus from rupture.

Variation in Size: Change in size of the tumor associated with a bloody nipple discharge is almost pathognomonic of a papillomatous cyst.

Pathologic Examination: There usually is a cyst with one or more papillomas, a thin wall and no invasion. Frequently there are multiple cysts and about these all types of epithelial proliferation, duct adenoma, cystic adenoma and nonencapsulated adenomatous areas, with associated hemorrhage into the tissues or a superimposed infection, these giving a fibrous proliferation.

Malignant Group.—A large percentage of the cases in the malignant group gave the picture of cancer, clinically, grossly and microscopically.

Origin of the Malignant Tumors: The cancer may apparently arise from a papillomatous cyst, or occur in a breast the seat of one or more of these tumors.

Duration: The duration usually is short, but in one case the tumor was present for thirteen years, suggesting a benign growth for eleven years, with malignant change about the time of or following incision. No other patient gave a history that would suggest malignant change in a benign tumor.

Size: The tumor was large in a much higher percentage (70 per cent) of cases than in the benign group (38 per cent) despite their much shorter average duration.

Infection: These cystic tumors with a slow or intermittent discharge are very prone to infection. This in the benign cases may give the clinical picture of malignancy with lymph gland enlargement.

Pain: There was pain in 41 per cent of the benign and in 67 per cent of the malignant cases. This symptom brings the patient earlier for operation than tumor or nipple discharge.

Radical Treatment in the Past: In an unusually large number of cases of the benign group the patients have been submitted to radical treatment—40 per cent to amputation of the breast and 38 per cent to the radical operation with removal of the pectoral muscles and axillary contents for cancer. Most of the diagnoses of "cancer" or "suspicious of cancer" have been made at exploratory incision.

Removal of the Breast Only: This operation for a case "suggestive of cancer" is unjustifiable, being too little for cancer and too much for a benign tumor not involving the greater part of the gland.

Diagnosis: Clinical observation is conducive to more accurate diagnosis than is exploratory examination. The character and attachment of the cyst wall and pedicle of the papilloma are a more reliable aid in the diagnosis of malignancy than the cyst contents.

At the present time, since the patients come under observation earlier, making the diagnosis of malignancy more difficult, one is more apt to find cancer at the exploratory excision. The tumor should be excised and then thoroughly examined rather than explored.

Ultimate Results: Of the benign group 65 per cent of the patients were followed for from one to twenty-two years and none developed cancer. This, together with the fact that a large percentage of the patients who suffered from malignancy, died of recurrence, is offered as proof of the correctness of this division into two groups.

The malignant tumor is not cancer of a relatively low grade of malignancy. This impression has been founded on a study of cases of the benign tumor incorrectly diagnosed and placed with the cancer group.

REPORT OF CASES

For those who desire to study this question critically the following report of cases may prove helpful.

Group I.—Four cases have been removed from the malignant to the benign group, and thought to have been unquestionably diagnosed wrongly at first. In addition to these, so many other cases have previously been reclassified as benign, and the original mistakes in diagnosis at the present time are so evident, that to print reports of all these becomes superfluous.

CASE 1.—A white married woman, aged 71, complained of a burning sensation in the left breast of four weeks' duration. Examination showed a hard, indurated mass, about the size of a walnut, just outside the nipple, with no other evidence of malignancy in the nipple, skin or axillary glands. A complete operation for cancer was performed.

Pathologic examination showed a cyst, 2 cm. in diameter, near the nipple, filled with a bloody, jelly-like material, on removal of which the wall was seen to be lined with a ragged growth. There was no apparent infiltration outside the cyst wall. Microscopic examination showed the wall composed mostly of granulation tissue, with some evidence of a papilloma. Sections through the thick part of the wall of the cyst showed granulation tissue and papilloma, with the basement membrane of the duct gone. It was thought at the time to suggest carcinoma, and is now thought to be a papilloma with infection. The glands showed no metastases.

The patient, when last heard from two years after operation, was well.

CASE 2.—W. F. M., a woman, aged 45, had a bloody discharge from the left nipple occurring at intervals for eleven months. A tumor the size of a walnut was noted for three months with gradual increase in size. There was no pain. The positive physical findings were a firm, non-tender, irregular mass, about 6 by 4 by 4 cm., freely movable over the chest wall and fairly movable through the breast tissue, with some atrophy of the subcutaneous tissue and with slight dimpling of the skin with displacement of the tumor. The left nipple could not be pulled out quite as far as the right, and the left breast was at a little higher level. The lymph glands were negative. A complete operation for cancer was performed. No note about an exploratory incision was made.

Pathologically, there was a firm, fibrous tumor, showing a smooth walled cyst containing blood. At one end was another tumor and through this were numerous channels from 1 to 3 mm. in diameter, some filled with blood, and others containing a granular, cellular tissue. In sections one sees the ductlike spaces filled with epithelial débris, and in some a distinct papilloma. At the time this growth was thought to be suggestive of malignancy, but is now thought to be benign. The patient is well at the present time, eight years after operation.

CASE 3.—C. F. M., a woman, aged 50, had a lump in the right breast of one year's duration. There had been a slight increase in size, and pain for nine months. No nipple discharge was noted. Examination showed the right breast hanging 1.5 cm. higher than the left, with a fulness over the lower part. The skin over this was a trifle shiny and below this was a small dimple. The mass was hard, irregular and very tender. The glands were negative. Clinically the cyst was benign.

Exploration was done and a complete operation for cancer performed.

Pathologic examination showed a tumor with three distinct lobules, each with a distinct wall. Within the cysts was hemorrhagic tissue, having a papillomatous arrangement. Microscopically, it showed a papilloma and seemed to be infiltrating outside the cyst wall. A note says that it would have to be called histologic cancer, though all similar cases had shown no metastases to axillary glands and all the patients had remained well. The glands were negative. It is now thought to be benign and not an invasive tumor.

The patient was well when last heard from in 1920, six years after operation.

CASE 4.—W. F. M., a woman aged 76, had a tumor for from twenty to thirty years which had increased gradually in size. No pain had been present until a

watery discharge from the nipple began six weeks before admission; there had been some pain since. Ulceration had been present for three weeks.

The nipple had entirely disappeared. An area of skin 8 cm. in diameter over the tumor was purplish, red, thin and adherent and ulcerated at the most forward point. Beneath this was a hard, irregular, nodular mass with a cystic center. From the sinus exuded a purulent discharge with white flakes of broken down "carcinoma." The remainder of this breast and the other breast were normal. There was a hard, freely movable lymph gland the size of a chestnut in the lower axilla. Clinically, the case was malignant.

The breast only was removed on account of the age of the patient, and the extensiveness of the condition.

Pathologically, the mass was definitely encapsulated, and there were numerous papillomatous growths in the cyst. Microscopic examination showed benign papillomas, infection, and what at that time was considered as adenocarcinoma. This area we now consider as a benign, cystic adenoma.

It has been impossible to trace this patient.

Group II.—Instead of an attempt to make a composite picture of an indefinite classification, the five cases in which the diagnosis is doubtful are given so that they can be read in detail. Certainly most of these cases are benign, since in general when pathologists disagree or are uncertain about malignancy the clinical course is more that of a benign condition.

CASE 5.—W. F. S., a woman, aged 47, had a tumor of the left breast of one year's duration, which had a bloody discharge from the nipple for eighteen months. No pain was felt, the tumor was irregular, nodular, the size of a chestnut, with dimpled skin and nipple elevated. A complete operation for cancer was done.

Pathologic examination showed a tumor about the size of a twenty-five cent piece, with remains of a cyst wall and suggesting infiltration in places. The tumor had the appearance of hemorrhagic medullary carcinoma, with the hardness of cancer. Microscopically it was said to be medullary carcinoma with minute cyst formation. The tumor was circumscribed. In some places it had a definite papillomatous arrangement. The glands showed no metastases.

To me this is definitely not medullary carcinoma, and I would call it benign. Bloodgood calls it a borderline group tumor.

The patient is well at present, two years after operation.

CASE 6.—W. F. M., a woman, aged 44, had a tumor present for six months, which rapidly enlarged to the size of a small orange, subsided under local applications with relief of the pain present during the distention. There was an associated discharge from the nipple.

Examination showed a nodule 2,5 inches (6.2 cm.) in diameter just above and to the outer side of the nipple. It had the hardness and irregularity of cancer, with slight atrophy of the subcutaneous fat. A complete operation for cancer was done.

Pathologic examination showed a cyst with smooth walls except for a thickening in the wall toward the nipple suggesting medullary carcinoma or adenocarcinoma, or possibly the base of a papilloma; but if the latter, the papilloma had disappeared. Microscopically it was said to be "typical of the adenocarcinoma of the papillary type." The lymph glands were negative.

Sections showed only the papilloma that Bloodgood says is hard to differentiate from cancer. To me it is more suggestive of a benign condition, though it is very hard to differentiate when only the intracystic growth is given.

The patient wrote in 1913, four years after operation, that she "is feeling fine, and the operation is a success in every way."

CASE 7.—W. F. M., a woman, aged 65, had a tumor of the left breast about the size of a robin's egg when first noticed seven months before admission. It was a slow growth until about one month before admission, since which time it has been rapid. The patient had had great anxiety and this was thought to have caused considerable loss of weight. On examination she was somewhat emaciated and had a tumor of the left breast the size of a hen's egg, firm, freely movable, not tender and with no change in the skin, nipple, axillary glands or subcutaneous fat. Amputation of the breast, without the sheath of the pectoral muscle, was done and axillary dissection for cancer.

Pathologic examination showed a cyst, divided into two compartments, with a wall from 1 to 3 mm. thick, except next to the septum, where it was about 2 cm. thick and composed of soft, friable tissue. A few calcareous deposits were present. Microscopically it was called an adenocarcinoma.

In sections taken from the thickened septum and papilloma Bloodgood diagnosed cancer. To me they show a dense fibrous tissue with scattered clumps of epithelial cells, which under the dissecting microscope seems to belong to the papilloma with areas of fibrosis. I am inclined to consider it benign.

The patient died eight years after operation, without further trouble. The registered cause of death was "uremia, secondary to an interstitial nephritis; and pernicious anemia, the latter recognized one year before death."

CASE 8.—W. F. S., a woman, aged 64, had a lump the size of a thumb in the upper outer quadrant of the left breast. It had been noticed six months before admission. There was no pain or tenderness. There had been rapid recent growth.

Examination showed a tumor 7 by 7 cm., irregular, hard and covered with large nodules. The nipple was normal, the skin tense, but not bound down, the veins large and prominent, and the whole tumor freely movable over the chest wall. There were many small nodules over the mass, some of them fluctuant. They were tender on palpation. No enlarged glands were noted. An exploratory incision was made and a complete operation for cancer was performed.

Pathologic examination showed a cyst containing a hemorrhagic grumous material, and a "definitely carcinomatous nodule on one portion of the wall;" otherwise the wall was smooth. Axillary glands were not enlarged. Microscopically it was said to show adenocarcinoma in the wall of the cyst. The axillary glands were negative. To me at the present time there seems a possibility of the growth being a papilloma, with infection superimposed.

The patient was well up to 1919, thirteen years after the operation, except for paralysis which had been present since 1915.

CASE 9.—W. F. M., a woman, aged 27, had a tumor of nine months' duration. It was the size of a walnut when first noticed; had a gradual growth for seven months, and a rapid one for the last two months, with much pain in the breast and arm. There was an associated discharge from the nipple for nine months. Examination showed a tumor occupying the outer hemisphere pressure on which caused a discharge of a rusty colored fluid from the nipple. The axillary glands were enlarged. The nipple was not retracted. A complete operation for cancer was done.

Pathologic examination showed a cyst with an intracystic papilloma. It was diagnosed as malignant, though there was no microscopic evidence to confirm this.

The patient died three and one-half years later. A note was made that death was not due to cancer and that there had been no return of the trouble.

Group III.—The two cases of intracanalicular fibro-adenoma ran a clinical course similar to that of true papilloma, and on casual gross examination could well be confused with it. They have likewise been classified with this type of tumor, present the same problems, and in both of these cases malignancy was originally diagnosed.

CASE 10.—The revised diagnosis in this case was intracanalicular myxoma growing in a cyst and suggesting an intracystic papilloma. The first diagnosis had been a benign growth of the breast, a papillomatous cyst of the intracanalicular type. The adenomatous part showed carcinoma. (The "carcinoma" was afterward erased and "benign" written over it.)

W. F. S., a woman, aged 26, had a tumor which was first observed eight years before admission, when the patient was 18 years of age. With the first pregnancy eighteen months before admission, this breast secreted no milk but there was a more rapid growth of the tumor. Her second pregnancy was of seven months' duration, and the tumor had grown quite rapidly during this time. Four months before admission a sinus formed, which was thought to be tuberculous. The entire breast was removed without axillary dissection. No note was made as to the discharge from the nipple, but the cyst did not contain blood after the operation.

Pathologic examination showed a sinus in the skin, leading down to the cystic cavity, which had a smooth wall and contained a papilloma, nodular in type, about the size of an orange, and having the appearance of the intracystic growth of an intracanalicular myxoma. There was no infiltration beyond the wall.

Microscopically areas with irregular cells were seen and some cellular areas which might be suggestive of early malignancy. A note by Bloodgood later stated that this area marked "suspicious of malignancy" showed distortion due to a chronic inflammatory reaction and was benign. Study at the present time shows a typical intracranalicular myxoma with a chronic inflammatory reaction, manifested by a quite marked round cell infiltration and an occasional polymorphonuclear cell. There are remnants of epithelial structures, the cells having more the appearance of breast acini in infected tissue, and through these areas there are quite numerous small, and apparently newly proliferated blood vessels with large endothelial cells. Certainly the picture does not suggest carcinoma.

CASE 11.—The diagnosis was benign tumor of the breast; intracanalicular myxoma, with a large pedunculated tumor, projecting into a cyst, suggesting an intracystic papilloma.

W. F. S., a woman, aged 22, had a tumor in the upper outer quadrant of the left breast of two years' duration. She had pain for two months, during which time the tumor had grown rapidly. The tumor was excised under local anesthesia. It contained blood tinged fluid and a cauliflower-like growth attached to the cyst wall. The operator, being in doubt as to the nature of the condition, then removed the entire breast, but no other lumps were found, and he states that the axillary glands were not palpable. The specimen was received with the question, "If this is cancer should the complete operation, with removal of the pectoral muscle and axillary dissection, be done?"

The cyst was small, 3 by 5 cm. in diameter, and was said to contain blood tinged fluid; it was excised with a small zone of surrounding tissue. Projecting from one side was a polypoid, cauliflower-like growth. The wall of the cyst was otherwise smooth, glistening and quite loosely attached to the surrounding breast. A microscopic section through the base of the pedicle showed that there had been no invasion of the surrounding tissues, and further sections proved that there were other smaller cysts, similar to the larger, and with pedunculated growths from the wall. The growth was a typical intracanalicular myxoma, with no evidence of malignancy or suggestion of invasion.

CARCINOMA OF THE MALE BREAST

CLINICAL AND PATHOLOGIC STUDY

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HISTORICAL

Ambrose Pare (Paris, 1510-1590), Thomas Bartholinus (Copenhagen, 1616-1680) and Ledran (Paris, about 1778) are said to have written of carcinoma of the male breast, but it has not been possible to consult these articles. About 1820, articles on the subject began to appear in medical journals, especially in the *Lancet*. Liston (Lancet, 1838), one of the notable earlier reporters, while operating on a man said: "Those who witnessed the operation observed that I was at no pains to preserve integument." A somewhat naive remark which I think might well receive more consideration today. From 1820 to the present day, articles have frequently appeared, especially in the French, English and American journals. German contributions have, singularly, been infrequent. Horteloup [1] collected seventy references to diseases of the breast of all kinds in man. Velpeau [2] mentions, without going into detail, ten cases of carcinoma in men in about 2,000 cases of various conditions of the breast. In 1844, Walsh,[3] quotes Velpeau as saying that he has "never seen and neither do other writers quote any examples of the dissemination of these tumors (i. e., male breast carcinoma), or of their being reproduced in the viscera or other parts of the economy in men as in women." Velpeau, in 1854, admits this as his previous opinion, but says, "I would not say this as before . . . as I have several times had occasion to prove the contrary since."

The earlier writings were largely reports of single cases. The first systematic study of carcinoma of the male breast was published in 1883 by Paul Poirier.[4] Poirier's introductory paragraph is such a fine example of French completeness and clearness that it is quoted in full.

> The condition more often begins in the second half of life, 45 to 65 years. It begins ordinarily as a small limited induration, under or near the nipple. It remains in this state sometimes for a considerable period without causing appreciable pain and without affecting the general health. Then suddenly, after six months to five years, the tumor increases in volume and soon is the

1. Horteloup: Thëse de Paris, 1872.
2. Velpeau: Maladies du Sien, 1854.
3. Walsh: Anatomy, Physiology and Treatment of Cancer, 1899.
4. Poirier: Paris Thesis, 1883.

size of a nut or an egg. The skin becomes adherent and dimpled. The nipple retracts and becomes buried. The tumor becomes hard and nodular. Ordinarily about this period one or two glands appear in the axilla, sometimes they are connected to the tumor by a nodular cord. Quite often one now sees small nodules or tubercles appearing around the tumor, they have the characteristics of the principal mass. The patient now begins to complain of lancinating pains. Then only the skin, distended and adherent to the tumor, reddens and perforates, there is ulceration; the ulcer is excavated, the borders hard, the base is firm, it increases slowly and it may be the seat of hemorrhages. Such is the picture which presents ordinarily. The general health is good for a long time, progress is always slow. This clinical type corresponds to the anatomical form which we have described under the name of scirrhus carinoma. But other cases with a different histological structure progress more rapidly. They are much more rare.

Another elaborate study by Schuchardt [5] appeared the following year, and in 1894, the subject was again discussed at length by Williams.[6] This is the only textbook I have seen in which carcinoma in the male breast receives any systematic notice.

The present inquiry is based on an exhaustive study of the literature. All titles in the *Surgeon General's Index* and the *Index Medicus* have been personally consulted, with the exception of about a dozen articles in unavailable journals or in impossible languages. The total references personally consulted number 166. These articles have yielded a total of 264 cases reported in sufficient detail to be interesting. Cases merely mentioned and not accompanied by data have not been included. The original reference has been consulted in nearly all of these cases; all of the notes have been indexed, and duplication carefully avoided. In addition to the cases in the literature, I have compiled from hospitals and personal communications a total of 154 cases. Thus, a total of 418 more or less well detailed reports forms the basis of this study. Slides of seventy-nine cases have been borrowed or restudied in various laboratories.

STATISTICAL STUDY

In order to increase the interest of the statistical data, comparisons will be made with statistics concerning carcinoma in the male breast by Williams [6] and with statistics for the female breast by Lane-Claypon.[7]

In the present compilation, the side is mentioned in 336 cases as follows: right 163, left 170, bilateral 3; Williams reported: right 38, left 33; Lane-Claypon reported in women (twelve different countries): right 6,907, left 7,002. It would appear therefore that in both men and women there is a slight preponderance for the left side.

5. Schuchardt: Arch. f. klin. chir. **31**:1, 1884.

6. Williams, W. Roger: A Monograph on Diseases of the Breast, London, 1894.

7. Lane-Claypon: Reports on Public Health, Medical Subjects, no. 28, Ministry of Health, London, 1924.

The age at the time of observation is given in 401 cases. The average age is 54.2 years. Lane-Claypon does not give the average in her large collection of statistics on women, but in table 1 she does give an elaborate classification by semidecades and a comparison of the data on men.

It has frequently been noted by others that carcinoma of the breast develops later in men than in women. This apparently is borne out by the foregoing. Most cases occur in women between the ages of 45 and 49; in men, between the ages of 60 and 64; about one half of the women and about two thirds of the men are over 50.

The youngest patient among the men is difficult to determine with certainty. Blodgett [8] gives a brief report of a case in a boy, aged 12. The duration of the condition and the microscopic report were not given. An operation was performed, and the patient was well five years

TABLE 1.—*Ages at Operation (Or Coming Under Observation of the Reporter) Percentages for Each Quinquennial Period.*

	Age Periods															
	10 to 14	15 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79	80 to 84	85 to 89	90 to 94
Lane-Claypon 8,053 women	1	1	0.1	1.0	3.9	8.4	14.7	18.3	17.2	13.4	11.2	6.8	3.4	1.2	0.2	0.2	...
Present series 401 men	0.5*	0.2*	1.5*	0.7	1.5	5.7	8.7	14.0	13.2	16.2	17.2	9.2	8.0	2.0	0.75	0.25	2.5

* These cases in very young patients are discussed below.

later. Simmons [9] reports a case in a boy, aged 13, who was operated on when he had had a carcinoma for one year. The pathologic diagnosis was adenocarcinoma of the breast of a medullary type. The patient was well, January, 1926, nine years after the operation. Bryan [10] reports a case in a boy, aged 14 years and 8 months, who developed a tumor following a blow by a golf ball. After a duration of six months the patient was operated on. A pathologic diagnosis showed adenofibroma with "distinct scirrhus carcinoma in a scattered area of active profilteration." The patient was well in 1926, thirteen years after operation. None of the foregoing cases sound convincing, and as slides are not now available, they should be considered as not proved.

Coley [11] reports a more definite case in a man, aged 22. After a duration of three years an operation was performed. There was a prompt recurrence of the tumor followed by a second operation and a

8. Blodgett: Boston M. & S. J. **136**:611, 1897.
9. Simmons: Adenocarcinoma, J. A. M. A. **68**:1899, June 23, 1917.
10. Bryan: Surg. Gynec. Obst. **18**:545, 1914.
11. Coley, W. B.: Ann. Surg. **31**:741, 1900.

second recurrence. The condition was inoperable when the patient was seen by Coley. A nodule was removed, and the section examined by Braxton showed carcinoma. The condition began when the patient was 19.

The youngest patient in the present series whose case was definitely proved was operated on by Deaver (personal communication). The patient first noticed the growth when he was 23 years old. The primary operation was by another surgeon. The growth promptly recurred and Deaver's operation was for the recurrence two years after the onset of the growth. A follow-up record was not made. The tissue, removed by Deaver and examined by Reiman, was found to be carcinomatous. This slide is in the group in my collection now being restudied, and it is undoubtedly a scirrhus carcinoma of high malignancy. The axillary glands were involved. The tumor was not ulcerated.

The case of the oldest man, aged 91, is recorded by Lunn.[12] The duration of the condition is not given, and the patient died after the operation.

AGE INCIDENCE

The age of the patient when the tumor was noticed is given in 325 cases; the average age is 52.6 years. In computing this average, cases in which the alleged duration is twenty years or more have been omitted. It is probable in these that the information was incorrect or that a benign tumor became malignant at an unknown date. When the age at which the tumor was noticed is analyzed by age periods, the period of greatest frequency is again from 60 to 64 years. The second most frequent period is from 55 to 59 years. The table according to frequency at age periods is practically the same as table 1, so that the table based on the age when the tumor is noticed need not be repeated.

DURATION OF TUMOR BEFORE COMING UNDER OBSERVATION

The time the tumor was observed before coming under the reporter's observation is noted in 342 cases. The average period is 2.4 years. It has been said that men with tumors of the breast delay longer before consulting a physician than women. This study does not show any essential difference; the delay is perhaps greater than with women at present, but many of these cases were reported before the present interest in cancer developed—many before the days of antiseptics.

Table 2 shows that nearly half of the men apply for treatment during the first twelve months. It is doubtful that women equal this even now.

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12. Lunn: Tr. Path. Soc. London, **48**:247, 1897.

The cases in which a long duration of the tumor is alleged are of especial interest. The five cases in which the duration is from twenty to thirty-four years are given in detail in table 3.

In these cases in which the patient's condition was of long duration it is more probable that the tumor originally noticed was benign and changed to carcinoma later. Occasionally the course is slow in cases that are definitely cancerous from the beginning. Even so it is hard

TABLE 2.—*Stated Duration of Tumor at Time of Observation by Periods of Time*

Time	Percentage of Total
0 to 6 months	23.3
7 to 12 months	23.3
13 to 23 months	7.9
2 to 3 years	25.8
4 to 5 years	8.5
6 to 9 years	4.4
10 to 14 years	3.0
15 to 19 years	1.4
20 to 34 years	1.4

TABLE 3.—*Details of Cases With an Alleged Duration of From Twenty to Thirty-Four Years*

Reporter	Age at Observation	Alleged Duration, Years	Beginning of Rapid Growth	Ulcerated	Axilla Involved	Slide Verified in This Study	Type	Estimation of Malignancy	End Result
Auchincloss.. (New York)	53	20	1 year	No	Yes	Yes	Scirrhus	Medium	Well 27 months after operation
Roberts..... (Toronto)	60	25	Pain last 2 years	No	Yes	Not available	.....	.....	Died 6 years after operation at age 76; said to be free from cancer
Greenough... (Boston)	57	25	.....	Yes	Yes	Not available	.....	.....	Inoperable; died
Warfield..... (Milwaukee)	47	26	3 years	Yes	Yes	Yes	Scirrhus muscle involved	High	Died 5 months after operation; metastases
Jeanneney... (Bordeaux)	61	34	2 years	No	Yes	Yes	Squamous epithelioma	Low	Well 26 months after operation

to believe that in four of these cases the condition should still have been operable twenty, twenty-five, twenty-six and thirty-four years, respectively, after first being noticed, if the tumors were carcinomatous from the start. Robert's patient gave the following history: "twenty-five years ago the nipple began to draw in and it gradually entirely disappeared and the skin grew over it. After fifteen years a wart-like mass appeared where the nipple had been and slowly grew till it was the size of a finger nail. It was not ulcerated or cracked."

The three slides of these long-standing cases which have been restudied do not indicate a previous benign tumor.

The only case history that indicates a previous pathologic condition was one of A. C. Wood, Philadelphia (personal communication). The patient, aged 47, had a tumor of unknown duration, said to have developed in a "port wine mark." A microscopic diagnosis showed basal cell carcinoma. The slides are not available now and the end-result is unknown.

RACE INCIDENCE *

Sirrha [13] reports a case in a native East Indian, aged 35, in whom the condition was of two months' duration. The tumor was ulcerated, but the axillary glands are not mentioned. An operation was performed. The end-result and microscopic report are not given. Welch [14] reports a case, his report is accompanied by good photographs and slides. The patient was a Kikuyu, British East Africa, aged 42. The duration of the tumor was two months. It had ulcerated, and the axillary and supra-clavicular glands were involved. An operation was performed. The microscopic diagnosis was adenocarcinoma. The end-results are not given. These are the only two cases found in the literature that did not occur in Caucasians or in American negroes. Numerous cases are reported by American surgeons in negroes. It has been impossible to determine anything in connection with incidence and proportion of white and black populations in the towns represented. The cases are so numerous that presumably the negroes show about the same general incidence as the Caucasians.

CHARACTERISTICS OF CARCINOMA OF THE BREAST

Ulceration.—Naturally, ulceration of the skin at time of observation is more common in men than in women. This point is mentioned in 306 cases; in these, ulceration was present in 162 patients or more than one-half—a higher figure than one would expect. In the cases in which ulceration is not mentioned it probably did not occur. A comparison with the total number of cases therefore is presumably more correct. Of the total reported in this collection, ulceration is definitely stated to be present in 38 per cent. Ulceration does not seem to follow any law. In some cases it is the first symptom noticed; in other cases, it occurs within a month after the tumor is first noticed. In many cases the

* Since this paper was written a report by Ludlow (*China M. J.*, Dec. 1925) has been found. Ludlow's patient was a native Korean, aged 70, with a tumor of seven years' duration which was ulcerated. The axillary glands were not involved; a radical operation was performed. Two years and three months later (September, 1925), the glands were removed from both axillae; no later note. Dr. Ludlow kindly sent on slides from each axilla. They are unquestionably adenocarcinoma of low malignancy.

13. Sirrha: Indian M. Rec. **10**:146, 1896.
14. Welch: Lancet, **1**:1319, 1914.

tumor has been present several years without ulceration. Table 3 shows three patients with tumors of twenty, twenty-five and thirty-four years' alleged duration which were not ulcerated, clinically. The size of the tumor does not seem to influence the question of ulceration. Sumner (personal communication) reports a tumor the "size of a base ball" which was not ulcerated. Jeanneny shows a profile photograph of a tumor that must have been just as large, which also was not ulcerated. Ullman reports a tumor "larger than a baseball" which was not ulcerated.

Axillary Involvement.—The axilla is mentioned in 331 cases. It was involved in 228 or more than two thirds of the cases noted. The same objection to this comparison holds as in ulceration. Of the total 418 cases, the axilla is definitely stated to be clinically involved in 54 per cent. Microscopic examiation of the axillary glands is not mentioned often enough for analysis.

Trauma.—Unfortunately in the earlier abstracts of the literature a reference as to trauma was not regularly recorded, so that of the 264 cases in the literature note of a definite statement as to trauma is found only in eleven cases. It is equally unfortunate that in the blanks on which the communicated cases were received a question as to trauma was not included so that it is only casually mentioned in four cases. However, even with this meager data, I am impressed with the recollection that trauma is mentioned so frequently and so connectedly that it must be taken into consideration as a cause of carcinoma, at least in the male breast. In some cases there has been a constant trauma from tools as in shoemakers and carpenters, and in other cases there has been a single blow. Billroth reports a case of gunshot wound of the nipple. A carcinoma was noticed in the scar six months later. Lilienthal, New York (personal communication), reports a case in which a piece had been torn from the nipple fifteen years before. A crust formed, and the nipple became contracted. One case is reported following a sword thrust.

Murphy,[15] in discussing carcinoma in a man, said "In the breast carcinoma is very frequently the sequence of a mild trauma of single occurrence . . . It is the only place in the body where this is so." It is not improbable that in women, too, trauma would be accorded a more important effect if histories were more carefully taken with this point in view.

SYMPTOMATOLOGY

Symptoms in carcinoma of the breast in men differ from those in carcinoma of the breast in women only in frequency and in time of onset. Ulceration is more common and tends to appear earlier; pain is more common and appears earlier. A discharge from the nipple is

15. Murphy: Surg. Clin., Chicago, **3**:569, 1914.

a more frequent and a more dangerous signal in men than in women, and is more often bloody. It is more often possible to feel a cord of thickened lymphatics or glands along the axillary border of the pectoralis major. As the disease begins near the nipple, Paget's disease is more frequent in men. A few cases are reported in which it seems definite that a preexistent benign tumor has become malignant. Several cases have been reported which were bilateral at the first observation. Hansey [16] reports the case of a man, aged 61, who noticed a tumor in the left breast. Six months later he noticed one in the right breast. He was operated on and died eight months later of recurrence. In several others a "recurrence" has been noted in the other breast after operation.

PATHOLOGY OF CARCINOMA OF THE MALE BREAST

The form of the "normal" breast gland in man differs considerably. Sometimes it is an irregular conical or cuboidal mass about one half

Fig. 1.—Type of male breast closely corresponding in general topography to the female breast. This is a frequent type. The small black spots and lines represent ducts. A few of the ducts are slightly dilitated. Gland lobules or acini are not seen under the microscope.

inch (1.2 cm.) in diameter, and in form and general appearance it much resembles the first half inch of the duct-bearing cone in women as it lies directly under the nipple. The gland in men does occur as an exact miniature of the general shape of the gland in women. Figure 1 shows a good specimen of this kind. The gland tissue is represented by a broad based, low, conical mass about one and one-fourth inches (3 cm.) in diameter at the base and about three-eighths inch (0.9 cm.) thick at the apex. From its greater resemblance to the gland in women, it is probable that this type (fig. 1) represents the normal rudimentary male gland and that the first mentioned stubby type is a still more rudimentary variation.

16. Hansey: Wien med. Wchnschr. **49**:302, 1899.

Microscopically, the male breast consists of a compact mass of dense connective tissue. Areas of whitish breast tissue spreading irregularly through fat are not seen. The connective tissue is irregularly interspersed with ducts which are represented by thin lines of two layers of flattened epithelial cells rarely showing any tendency to lumen except near the nipple, unless there has been a chronic inflammatory process with partial or complete obstruction to the ducts, in which case they are dilated and much resemble the female ducts. Anything approximating the racemose type of gland structure with lobules and ultimate acini as in the female is not described in the literature, and I have not seen this in numerous male glands removed at autopsy.

The present pathologic study is based on the somewhat unique opportunity of studying, restudying and comparing during the past four years a collection of slides from seventy-nine cases of carcinomas of the male breast.

Perhaps the most striking impression obtained from the study of these seventy-nine cases is that the fully developed late cases are not distinguishable from the carcinomas in the female breast. It is doubtful whether a pathologist would suspect that any slide in the collection did not come from the female breast. This similarity of the developed type in the two sexes adds considerable weight to the generally prevailing view that even in women carcinoma of the breast usually arises from ducts. If, as is also generally agreed, acini are not found in the male breast, the point of origin of the cancer in both sexes is the same and naturally the end-product would be similar.

CLASSIFICATION

The classification suggested by McFarland [17] will be followed here. Except in a few cases in which classification was not practicable on account of poor sections or faded stain, the slides studied seem properly to be classified as in table 4. All subvarieties are grouped exactly as by McFarland, with the exception that basal cell tumors are added to group 6. The squamous and basal cell types probably arise from the more superficial portion of the ducts, as well as from the surface epithelium of the nipple.

It is not best to compare this table too closely with McFarland's table for women; in general, however, it would seem that the scirrhus, medullary and squamous types are more common in men. Carcinoma simplex is less common in men. The figures for adenocarcinoma are about equal.

Basal cell epithelioma of the nipple is not mentioned by McFarland. The only patient in the present series who had this type of carcinoma

17. Deaver and McFarland: Surgery of the Breast, Philadelphia, P. Blakiston's Sons & Co., 1917.

was operated on by Dr. John B. Deaver, the original diagnosis being made by Dr. John Reiman. The slide which was lent for the present study is characteristic. The patient was 57 years old, the duration of tumor before operation was not stated. The classification was low malignancy. The patient died eight years and one month after operation; the cause of death was unknown. A recurrence had not been reported.

The three malignant duct papillomas form an especially interesting group. David [18] reports eleven cases from the literature and one of his own in men. These cases were all apparently benign at the time of operation. Some recurred and were still considered benign. A few cases in men have been reported in the literature as malignant. This type of tumor deserves further study in both sexes. David says that about 10 per cent in both sexes become malignant. It would not be surprising if further study showed that all these tumors were malignant from the start or surely and early became so.

TABLE 4.—*Pathologic Classification of Seventy-Eight Cases of Carcinoma of of the Breast in Man*

	Total Number	Percentage
Scirrhus	38	49
Medullary	14	18
Simplex	3	3.7
Adenocarcinoma	13*	17
Gelatinous	3	3.7
Squamous or basal cell	7†	9

* Includes 3 malignant duct papillomas, 1 comedo type.
† Includes 1 basal cell.

The details in the three present cases so far as known are as follows:

CASE 1.—(Dr. J. P. Hoguet, N. Y., personal communication). A man, aged 57, had a tumor fourteen months before operation. Low malignancy was diagnosed from the section. The patient died four years and seven months after operation. There was a recurrence in the chest.

CASE 2.—(Dr. J. C. Bloodgood, Baltimore, personal communication). The patient, aged 35 at the time of operation, had had the condition for two years. Low malignancy was diagnosed from the section. The patient was well Jan. 25, 1927, one year and eight months after operation.

CASE 3.—(Dr. W. W. Propst, Scranton, Pa., personal communication). The patient, aged 82, had a tumor of twelve years' duration, which grew slowly for the first nine years, then rapidly. The section showed low malignancy. An operation was performed eight months before this article was written. The patient is still well. A photograph of a section of the entire tumor is shown in figure 2.

In all three of these cases the malignancy is definitely shown by marked permeation of epithelial cells in the walls of the cysts and surrounding tissues.

18. David: Ann. Surg. **75**:652 (June) 1922.

TABLE 5.—*Details of Proven Cases Alive at Present Writing (2-15-27)*

Date of Operation	Operator	Reference	Case Designation	Age at Operation	Pathologist	Pathologic Type	Axillary Glands Involved	Ulcerated	Malignancy Classification	Date Reported Well	Duration before Operation	Survival After Operation		Total Survival Before and After Operation		Slide Examined and Proved in Present Study
												Yrs.	Mos.	Yrs.	Mos.	
5/28/11	Hodge.....	Personal communication	W.F.M.	55	Eiman	Squamous cell	No	No	Low	2/15/27	3 mos.	15	9	16	0	Yes
10/ 4/13	Hubbard.....	Personal communication	M.N.	73	Whitney	Medullary	Yes	No	—	1/20/27	4 mos.	13	3	13	7	No
5/ 5/15	Mackenzie.....	Personal communication	N.	50	Bloodgood	Adenocarcinoma	No	No	Low	11/ ?/25	3 mos.	10	6	10	9	Yes
8/ ?/17	Berg.....	Personal communication	J.G.	..	Mandelbaum	Medullary	?	?	Medium	1/ ?/26	?	8	5	8	5	Yes
5/24/19	Deaver.....	Personal communication	J.F.	66	Reiman	Simplex	Yes	Yes	Low	1/19/27	15 yrs.	7	8	22	8	Yes
?/ ?/19	Judd.....	Surg.Gynec.Obst. 42 : 15, 1926	No. 5	45	?	?	No	?	High	1925	2 yrs.	5	?	7	?	No
5/20/20	Berg.....	Personal communication	K.	58	Mandelbaum	Medullary	?	?	Low	2/ ?/26	?	5	9	5	9	Yes
9/17/20	Lee.....	Personal communication	J.O'N.	42	Ewing	Adenocarcinoma	?	?	?	1/29/27	2 yrs.	6	4	8	4	No
1/19/21	Colvin.....	Personal communication	.....	57	?	Medullary	No	No	?	1/24/27	5 mos.	6	0	6	5	No
1/25/21	Wood.....	Personal communication	J.O'C.	70	?	Scirrhus	Yes	No	High	1/15/27	15 yrs.	6	0	21	0	Yes
6/22/21	Buchanan.....	Personal communication	J.C.	65	?	Simplex	No	No	Medium	10/14/26	2 yrs.	5	4	7	4	Yes
9/22/21	Adair.....	Personal communication	S.A.A.	64	Ewing	Medullary	No	No	Low	2/ 1/27	4 yrs.	5	5	5	9	Yes
?/ ?/21	Coley, B.....	Am.J.Surg. 40 : 90	C.B.	61	Jeffries	Scirrhus	No	No	High	2/ ?/27	6 yrs.	6	?	12	?	Yes
2/ 4/22	Cheever.....	Personal communication	.....	58	Wolbach	Scirrhus	No	No	?	1/20/26	1 wk.	3	5	3	5	No
5/ 3/22	Holman.....	Personal communication	J.L.	66	Bloodgood	Scirrhus	Yes	Yes	Low	6/23/26	3 yrs.	4	2	7	2	Yes
6/17/22	Moschowitz.....	Personal communication	S.	39	Mandelbaum	Medullary	No	No	Medium	1/18/27	Few days	4	7	4	7	Yes
1922	Judd.....	Surg.Gynec.Obst. 42 : 15, 1926	No. 17	60	?	?	No	?	High	5/ 3/26	2 yrs.	4	?	6	?	No
1/21/23	Whipple.....	Personal communication	W.M.	61	Clarke	Adenocarcinoma	Yes	No	Low	1/ 8/26	3 yrs.	3	0	6	0	Yes

2/ 3/23	Lee.....	Personal communication	G.D.C.	57	Ewing	Simplex	No	No	Low	9/18/25	9 mos.	2	7	3	4	Yes
2/23/23	Bloodgood.....	Personal communication	J.A.J.	56	Bloodgood	Scirrhus	Yes	No	Low	1/26/27	1 yr.	3	11	4	11	Yes
3/29/23	Berg.....	Personal communication	C.D.	43	Mandelbaum	Medullary	Yes	No	Low	9/27/26	6 mos.	3	6	4	0	Yes
5/ 1/23	Berg.....	Personal communication	S.P.	40	?	?	Yes	No	?	2/13/25	Few mos.	1	9	1	9+	No
7/17/23	Sumner.....	Personal communication	M.K.	42	Shaffer	?	Yes	No	?	1/24/27	5 wks.	3	6	3	7	No
7/ ?/23	Capwell.....	Personal communication	F.Q.	55	?	?	No	No	?	1/24/27	6 mos.	3	6	4	0	No
2/ 9/24	Cooke.....	Personal communication	A.W.J.	61	Bloodgood	?	Yes	No	?	1/14/27	1 yr.	2	11	3	11	No
2/20/24	Auchincloss.....	Personal communication	W.P.	53	Clarke	Adenocarcinoma	Yes	No	High	6/ 6/26	20 yrs.	2	2	22	2	Yes
5/13/24	Cameron*.....	Personal communication	.....	45	(?)	Medullary	Yes	Yes	?	9/15/26	1 yr.	2	4	3	4	No
3/29/21	Jeanneny.....	J.de med.de Bordeaux 54 : 794	No. 1	64	Sabrazes	Squamous cell	Yes	No	Low	5/27/26	34 yrs.	2	2	36	2	Yes
7/ 2/24	St. John.....	Personal communication	F.W.	54	Clarke	Scirrhus	Yes	No	High	1/28/26	6 wks.	1	6	1	8	Yes
8/23/24	Old.....	Personal communication	R.W.S.	58	Bloodgood	Scirrhus	Yes	No	Low	1/24/27	1 yr.	2	5	3	5	Yes
7/31/24	Woolf †.....	Personal communication	G.W.	74	?	Squamous cell	Yes	Yes	Low	2/ 1/27	1 yr.	2	7	3	7	Yes
9/ 9/24	Speed.....	Am.Surg.	M.C.	..	?	Scirrhus	....	....	High	3/ 2/26	1 mo.	1	6	1	7	Yes
1924	Judd.....	Surg.Gynec.Obst. 42 : 15, 1926	No. 7	..	?	?	Yes	?	Medium	1925	3 yrs.	1	?	4	?	No
2/ ?/25	Adair.....	Personal communication	M.R.	37	Ewing	Scirrhus	Yes	Yes	High	9/29/25	1 yr.	0	7	1	7	Yes
5/26/25	Boughton.....	Personal communication	J.A.S.	..	Bloodgood	Adenocarcinoma	Yes	Yes	Low	1/25/27	2 yrs.	1	8	3	8	Yes
8/20/25	Sullivan.....	Personal communication	J.H.G.	59	Roman	Medullary	No	No	Medium	2/ 8/27	9 mos.	1	6	2	3	Yes
9/ 5/25	Tannenbaum....	Personal communication	F.A.	74	Ewing	Scirrhus	No	Yes	High	12/28/25	1 yr.	0	3	1	3	Yes
9/15/25	Peck.....	Personal communication	C.McK.	53	White	Adenocarcinoma	No	Yes	Medium	1/25/27	6 mos.	1	2	1	8	Yes
1925?	Judd ‡.....	Surg.Gynec.Obst. 42 : 15, 1926	No. 14	48	?	?	Yes	?	High	1925 ?	2 yrs.	0	6	2	6	No
6/ 1/26	Morgans.....	Personal communication	E.M.	68	Thibaudeau	Scirrhus	Yes	No	High	1/26/27	4 mos.	0	7	0	11	Yes
6/18/26	Propst.....	Personal communication	M.B.	82	Mattas	Adenocarcinoma	No	No	Low	2/15/27	12 yrs.	0	8	12	8	Yes

* On Jan. 30, 1927, Dr. Cameron writes that this patient died of metastasis in mediastinum in October, 1926.
† On Feb. 1, 1927, Mr. Woolf writes that this patient is alive but in bad condition on account of local and mediastinal recurrences.
‡ January, 1927, Dr. Judd writes that this patient died of grippe one year and four months after operation.

Several points of especial pathologic interest are illustrated in the accompanying photomicrographs.

THE END-RESULT

The end-result is known in 163 cases. Forty-one patients were alive at a recent date; ten patients died after the operation. Accurate data as to the total duration in patients surviving operation have been obtained in 111 cases. The average survival in these is two years and nine months after operaion.

Of the known end-results in these cases, only thirty-one patients, or 19 per cent, have survived five years. It would seem therefore that in general the end-results in men are not so good as in women.

Table 5 gives the details of the forty-one cases in which the patients are still alive. The person who has survived longest was operated on by Dr. Hodge of Philadelphia. This patient is well and apparently free

Fig. 2.—Duct papilloma, carcinomatous, in a man, aged 82. Duration of condition was twelve years. He was operated on June, 1926; well February, 1927. Arrow indicates nipple. (Slide presented by Mattas.)

from cancer fifteen years and nine months after operation. The slide has recently been restudied by Eiman of Philadelphia and by me, but as it is faded a good reproduction cannot be made. The condition is unquestionably a carcinoma of the squamous cell type with low malignancy. The second longest survival is that of a patient reported by Hubbard of Boston as apparently free from cancer thirteen years and three months after operation. Unfourtunately, a slide of this case is not now available. The microscopic diagnosis was made by the late W. F. Whitney of the Harvard Medical School. Whitney was studying pathologic conditions of the breast with Warren in the 80's, and his opinion in 1913 should be accepted.

The third longest survival reported by Mackenzie of Auckland, N. Z., is that of a patient apparently free from cancer ten years and six months after operation. A slide of this patient shows that the condition is an adenocarcinoma of the comedo type of low malignancy (fig. 3).

The microscopic section of two of the patients surviving after five years (Wood and Coley) is classified as being of high malignancy. Both of these patients had an unusually long alleged duration before operation, fifteen and six years, respectively. It is probable that in patients with a tumor present so long before operation and surviving a long time after operation there is some factor present that cannot be appreciated with the microscope.

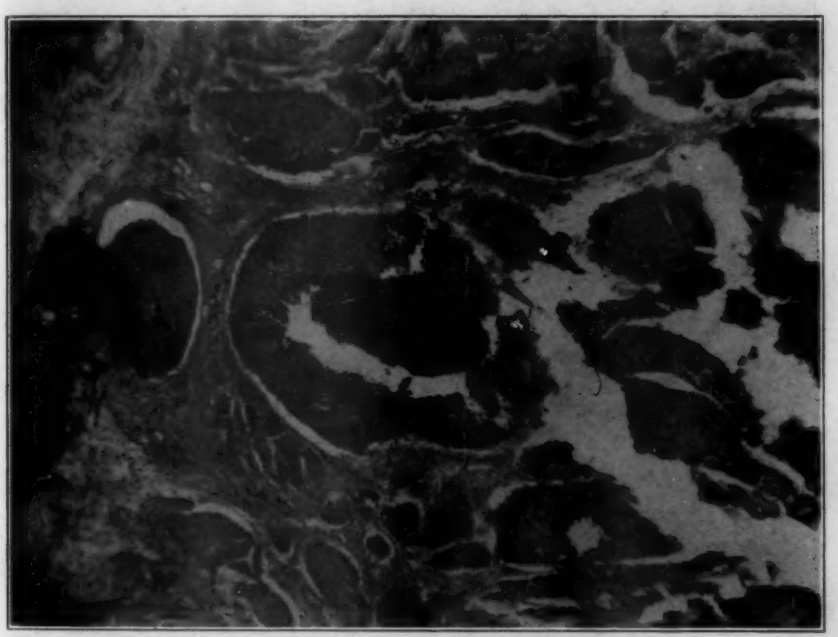

Fig. 3 (Dr. McKenzie's case).—Adenocarcinoma, comedo type, low malignancy. The patient, aged 50, had had the condition for three months; he was well and free from cancer ten years and five months after operation. (Slide lent by Bloodgood.)

A few other patients whose tumor was considered carcinoma have been well for a long time, but unfortunately the diagnosis cannot be proved. Willy Meyer operated on a man with a tumor of the breast who is well after twenty years. Neither a slide nor a pathologic report is available. Finsterer [19] mentions a case in a man, aged 24, who was followed twenty years after operation, and then he disappeared from observation. A pathologic report is not given, although Finsterer says

19. Finsterer: Deutsche Zschr. f. Chir. **84**:201, 1906.

that a microscopic examination was made. Correll of Easton has a patient who is alive ten years after the operation; however, the slide from this case is too faded to be of value.

Table 6 gives details concerning patients who died more than five years after the operation. The case of greatest interest is reported by Mitchell of Washington. A slide of this case is reproduced in fig. 4 and has recently been restudied by Bloodgood and myself. It definitely shows carcinoma. It is of the cylindroma type, and hence in McFarland's classification it falls into the adeno group. The malignancy classification is definitely low. This patient's physician was in

Fig. 4 (Dr. Mitchell's case).—Adenocarcinoma, cylindroma type. The patient had had the condition five weeks; he died twenty-two years after operation of heart disease. He was free from cancer. Same case as figure 5. (Slide lent by Bloodgood.)

close touch with him for many years. He is convinced that the patient remained free from cancer. Death was due to heart disease twenty-two years after operation at the age of 71. This is the longest recorded survival in which data of the case are definite and an unquestionable slide is still available. Figure 5 shows this patient fourteen years after operation. It is remarkable that another slide lent by Bloodgood is almost identical with the slide of Mitchell's case. It is even of lower malignancy. In this case the patient, colored, aged 69, had a tumor of five years' duration. The glands in the axilla were not palpable. The

TABLE 6.—*Details of Cases Dying More than Five Years after Operation*

Operator	Reference	Case Designation	Age at Operation	Pathologist	Pathologic Type	Axillary Gland Involved	Ulcerated	Malignancy Classification	Duration before Operation	Duration after Operation	Total Time Onset to Death	Slide Examined and Proved in Present Study	Note at Death
Mitchell	Personal communication	G.S.H.	49	Bloodgood	Adenocarcinoma	No	No	Low	5 weeks	22 years	22 years	Yes	Heart disease; cancer free*
Balloch	Wash.M.Ann. 7 : 8, 1903	H.M.	66	Graham	?	No	No	?	3 years	16 years	19 years	No	Cancer free
Gibson	Ann.Surg. 56 : 471, 1912	G.W.	62	Wood	Medullary	No	No	Medium	4 mos.	14 years	14 years	Yes	Details unknown
Finney	Personal communication	R.J.	48	Bloodgood	Adenocarcinoma	Yes	No	?	6 mos.	12 years	12 years+	No	Recurrence
Finsterer	Deutsche Ztschr.f. Chir. 84 :201, 1906	V.	57	?	?	Yes	No	?	2 years	11 years	13 years	No	Nephritis; cancer free
Bloodgood	Personal communication	F.F.	?	Bloodgood	Medullary	Yes	Yes	Low	3 years, 6 mos.	10 years	13 years+	Yes	Recurrence
Deaver	Personal communication	J.T.	67	Reiman	Adenocarcinoma	Yes	No	?	3 years	9 years	12 years	No	Heart disease; cancer free
Pollock	Tr.Path.Soc.Lond. 27 : 234	....	65	?	?	?	?	?	?	9 years	9 years+	No	Apoplexy; cancer free
Frazier	Personal communication	D.B.	66	McFarland	?	Yes	Yes	?	1 year, 6 mos.	8 years, 3 mos.	9 years, 9 mos.	No	Carcinoma of throat
Deaver	Personal communication	N.E.	57	Reiman	Basal cell	Yes	No	Low	?	8 years, 1 mo.	8 years, 1 mo.+	Yes	Details unknown
Greenough	Personal communication	W.S.S.	69	?	?	No	No	?	10 years	8 years	18 years	No	Recurrence
Truesdell	Personal communication	J.K.	62	Wood-Ewing	Simplex	Yes	No	Low	?	7 years, 1 mo.	7 years, 1 mo.	Yes	Recurrence
Roberts	Personal communication	J.T.B.	69	?	?	Yes	No	?	25 years	7 years	32 years	No	Cause (?) had obstinate sciatica for 2 years
Judd	Surg.Gynec.Obst. 42 : 15, 1926	No. 16	55	?	?	0	?	?	8 mos.	6 years	6 years, 8 mos.	No	Nephrectomy for hypernephroma; cancer free
Greenough	Personal communication	J.B.	52	?	?	No	Yes	?	1 year, 6 mos.	5 years, 6 mos.	7 years	No	Details unknown
Finsterer	Deutsche Ztschr.f. Chir. 84 :201, 1906	No. 8	63	?	?	Yes	Yes	?	2 years, 6 mos.	5 years, 3 mos.	7 years, 9 mos.	No	Details unknown
Lilienthal	Personal communication	M.O'S.	58	Mandelbaum	Scirrhus	Yes	Yes	High	?	5 years, 3 mos.	5 years, 3 mos.	Yes	Recurrence
Greenough	Personal communication	W.S.	75	?	?	Yes	Yes	?	4 years	5 years, 1 mo.	9 years, 1 mo.	No	Details unknown
Keyser	Lancet 1 : 1493, 1904	No. 4	48	?	?	No	No	?	3 mos.	5 years	5 years, 3 mos.	No	Recurrence
Douglas	Personal communication	W.G.	40	Wood	Scirrhus	No	No	Medium	1 year, 6 mos.	5 years	5 years 6 mos.	Yes	Recurrence

* The term cancer free expresses the best available clinical data. Cases were rarely under the care of the reporter at the time of death. An autopsy is recorded in only one case (Truesdell's).

patient died two years and eight months following the operation with enlarged glands in the axilla and internal metastases. It is possible that the difference in result is accounted for by the fact that the axilla was not dissected on account of the age of the patient and the apparent benignity of the tumor.

Study of table 6 shows that in men as well as in women recurrence can be the cause of death well after the fifth year period, as in Finney's and Bloodgood's cases in which recurrence caused death twelve and ten years, respectively, after operation. In both these cases death was possibly delayed by one secondary operation. In the twenty patients surviving five years, the condition at death is indicated in twelve; six were considered free from cancer, and six died of definite recurrence. Probably in one other case (Robert's) the patient died of recurrence.

End-Result According to Variety of Growth.—A study of the end-result according to the histologic variety is of considerable interest.

Fig. 5 (Dr. Mitchell's case).—Patient shown fourteen years after operation; lived eight years longer.

Table 8 shows the duration before and after the operation in the cases in which slides have been available for the present study. Ideas as to classification vary so much that it has not seemed profitable to make this analysis for all the cases reported. The present grouping has at least the advantage of having been made by a single observer.

Definite deductions must not be made from this small list of cases. Several interesting points, however, are indicated. The slower growth of the adenocarcinomas seems to be well shown by the decidedly longer time they exist before the surgeon is consulted. There is a similarity as to the time before the operation in other varieties except the gelatinous. There are only three in this group. This small number shows a long duration before operation and a short survival after operation. All three are dead. The duration after operation which is known in two is two years and four months, and ten months, respectively. The medullary, adenocarcinomas and squamous or basal cell

variety show the longest survival after operation and are surprisingly similar. The scirrhus type, as is to be expected, shows a short survival after operation. It is probable that the simplex variety would show a longer survival if there were more cases.

End-Result According to Differentiation (Greenough[20]*).*—Prolonged study has been given to the end-result in connection with the degree of differentiation as described by Greenough.

The sections from the seventy-nine cases studied have been grouped as to differentiation into three groups; high, medium and low malignancy. This study has lead me to agree with Greenough that it is best not to attempt to differentiate more than three classes. This is partly because I do not feel that I can divide my cases into four classes and partly because I feel that the division into four groups is finer than the traffic will bear. In actual practice one puts a section in the middle because one does not know in which end it should be put. Why split up a middle class thus formed?

TABLE 7.—*Showing End-Results Classified According to Variety of Growth*

	Total in Group	Average Duration Before Operation	Average Duration at Death After Operation	Alive at Present Writing
Scirrhus	38	1.7 years (26 cases)	2.4 years (18 cases)	6
Medullary	14	1.2 years (8 cases)	7.1 years (6 cases)	6
Simplex	3	2.2 years (3 cases)	1.9 years (1 case)	2
Adenocarcinoma	13	4.5 years (11 cases)	7.1 years (5 cases)	5
Gelatinous	3	3.2 years (3 cases)	1.5 years (2 cases)	0
Squamous or basal cell	7	1.7 years	7.2 years (4 cases)	2

Dr. A. P. Stout, of Columbia University, has also studied my collection of slides from this standpoint, and we have agreed as to the grade of malignancy in most cases. Where there has been a difference of opinion, Stout's classification has been accepted.

The number of cases of carcinoma in men studied in this group is almost equal to the number studied in Greenough's group of women. It is striking that in both groups the number of cases in each assigned to the low and high malignancy classes is practically equal, namely, for men, 30 low and 29 high; for women, 19 low and 21 high. There is a considerable difference in the proportion assigned to the medium group. In men 22 per cent were in the medium group, in women 45 per cent were in the medium group.

A study of table 8 shows that for this group of men the following points seem to be indicated:

(*a*) A difference is not shown in the groups as to the known duration of the tumor before operation.

20. Greenough: J. Cancer Research, 9:453 (Dec.) 1925.

(*b*) The time elapsing between operation and death shows a fairly regular fall in each group from those with a condition of low malignancy to those with a condition of high malignancy.

(*c*) The patients still alive after operation show a regular fall in each class from those with a condition of low malignancy to those with a condition of high malignancy. The same is true of the duration of the period of survival after operation in those dead.

(*d*) Regardless of whether they are dead or still alive, the number of patients passing the five-year period is as follows: low malignancy, 7, or 23 per cent; medium, 5, or 29 per cent; high, 2, or 6 per cent.

(*e*) The differences in clinical course betwen the medium and high groups are much more marked than the differences between those of the medium and low groups.

There have been a few cases in which these rules have not applied; that is, some cases in which the condition was classed as being of low

TABLE 8.—*Showing End-Results Classified According to Differentiation (Greenough)*

	Total in Group	Average Duration before Operation	Average Duration after Operation of Cases in Which Patient Is Known to Be Dead	Patients Alive at Present Writing
Low.....	30	2.7 years (22 cases)	5.6 years (10 cases)	13 (43.3%)
Medium.....	17	2.1 years (13 cases)	4.9 years (7 cases)	6 (35.5%)
High.....	29	2.1 years (25 cases)	2.0 years (13 cases)	9 (31.9%)

The patients still alive in the three classes have survived the following number of years:
Low malignancy.—1.50, 15.33, 1.08, 1.33, 10.00, 0.16, 2.58, 4.25, 5.75, 6.75, 4.16, 3.50, 2.00 years. Average, 4.1 years.
Medium malignancy.—4.58, 3.00, 0.50, 3.75, 8.50, 5.00 years. Average, 4.1 years.
High malignancy.—2.50, 3.00, 1.08, 5.00, 0.84, 1.58, 0.25, 5.00, 0.25 years. Average, 2.00 years.
The longest survival recorded (Mitchell's case noted above) in a proved case, is that of a patient who was definitely in the low malignancy group. He lived twenty-two years after the operation and died free from cancer.

malignancy have run a rapid course, and vice versa. However, the impression gained from this study is that it is of great value and that in general one can now fairly accurately indicate the clinical course from the microscopic picture and that even now the information gained from the microscope may be more correct than the clinical observation. For instance, in a case of Bloodgood's the known duration of the tumor was three years. It was "large," the skin was ulcerated, the muscle involved and the highest removed gland was involved. Surely the clinical data could not be worse, yet the malignacy group was low, and the man is alive and apparently free from cancer four years and two months after operation.

The discrepancies that now exist and the objections of some pathologists will probably largely disappear as pathologists more closely compare their slides with end-results.

The Effect of Muscle Involvement on End-Results.—This has been an interesting study, especially as from the closer position of the muscle it is involved earlier and more frequently than in women. A priori one

Fig. 6.—A section taken vertically through the middle of the nipple, in a patient, aged 66; shows involvement of the nipple, nearby skin, entire breast and muscle, low malignancy. Duration of condition three years; patient well and free from cancer four years and two months after operation. (Slide lent by Bloodgood.)

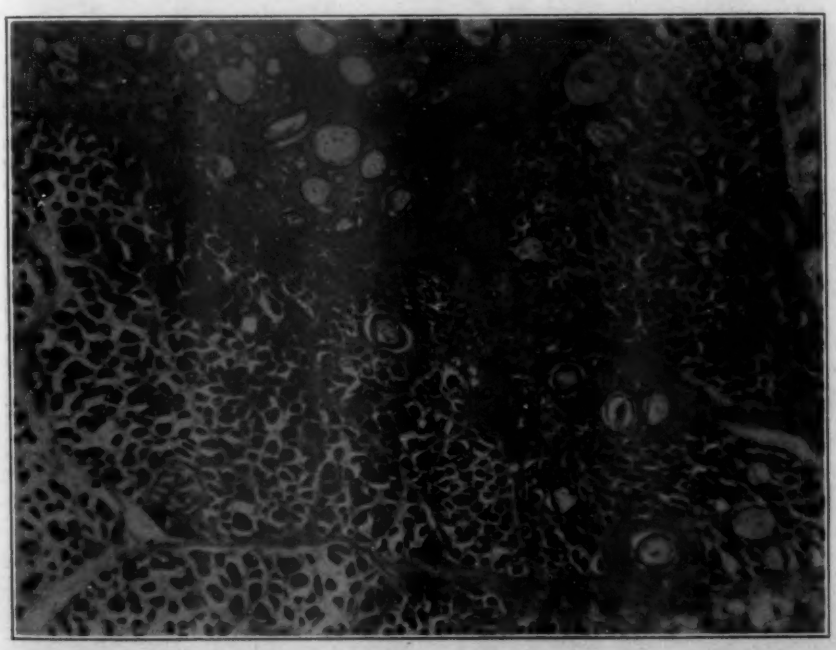

Fig. 7 (Dr. McConnell's case).—J. M. Research **22**:145, 1910. Tubular type of carcinoma, in a man, aged 54, showing marked involvement of pectoral muscle. Invading elements still maintain complete tubular structure. Condition discovered at autopsy. (Slide lent by McFarland.)

Fig. 8 (Dr. Deaver's case).—Basal cell epithelioma, low malignancy, in a man, aged 57. Duration of condition was unknown. Patient died eight years and one month after operation. (Slide lent by Reiman.)

Fig. 9 (Dr. Jeanneny's case).—Squamous cell carcinoma, low malignancy, in a patient, aged 64. Duration of condition was thirty-four years; patient well and free from cancer two years and two months after operation.

would infer that involvement of the muscle would greatly diminish the chance for long survival. Every physician now accepts it as a definite fact that massage rapidly spreads a primary growth. This could not be done better than by the continuous movement of a muscle on epithelial cells which have invaded its fibers. This is probably what led Heidenhain [21] many years ago to write that when a muscle is once involved, probably the whole muscle will be affected, and it should be removed entire, including the periosteum at its attachments.

In the group of seventy-nine cases in which slides were available for study, there was definite microscopic evidence of involvement of the underlying muscle in nineteen cases, 24 per cent.

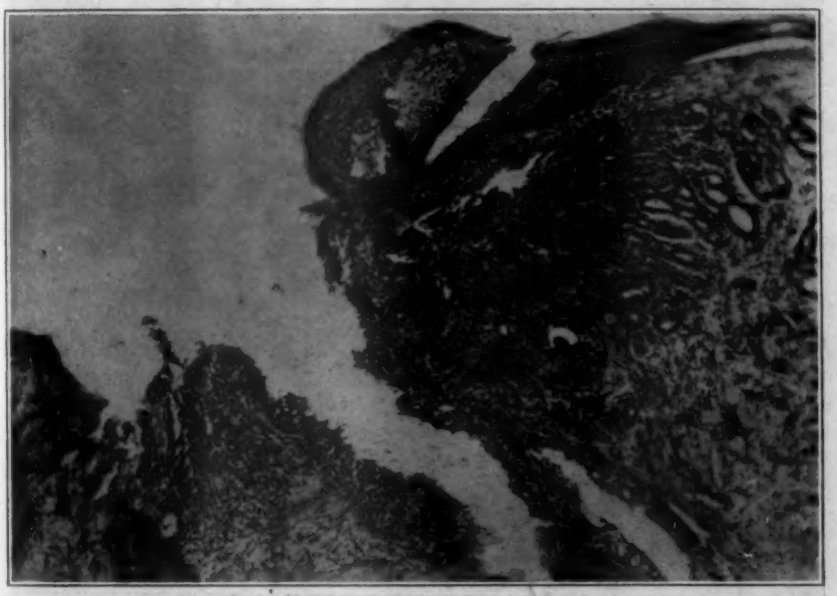

Fig. 10 (Moschowitz's case).—Carcinoma apparently arising at the mouth of the duct, deeper tissues show a medullary type, low malignancy, in a patient, aged 67. Duration of condition was ten years; two recurrences removed in first years, then patient disappeared from observation. (Slide lent by Mandelbaum.)

In cases in which the muscle was involved, the classification of the primary tumor is as follows: low 6, medium 3, high 10. The proportion of these cases in the high malignancy class is greater than in the entire group as 52 is to 38. The average time of death after operation for the low and medium classes combined is 3.3, for the high 2.2 years. There is one patient alive in each group after five years.

21. Heidenhain: Ann. Surg. **10**:383, 1889.

Taking the entire group (nineteen cases) with muscle involvement, the average time of the death of the patient is 2.8 years after operation. For 111 cases in the entire series (literature included), this average is 2.9 years. As far as one can judge from this series, involvement of muscle does not seem to shorten the end-result. It does not follow that this applies to women as in women the muscle is usually farther away from the primary tumor and its involvement indicates a wide extension from the original focus. Muscle involvement in women for the present therefore should be accepted as of much graver import than in man.

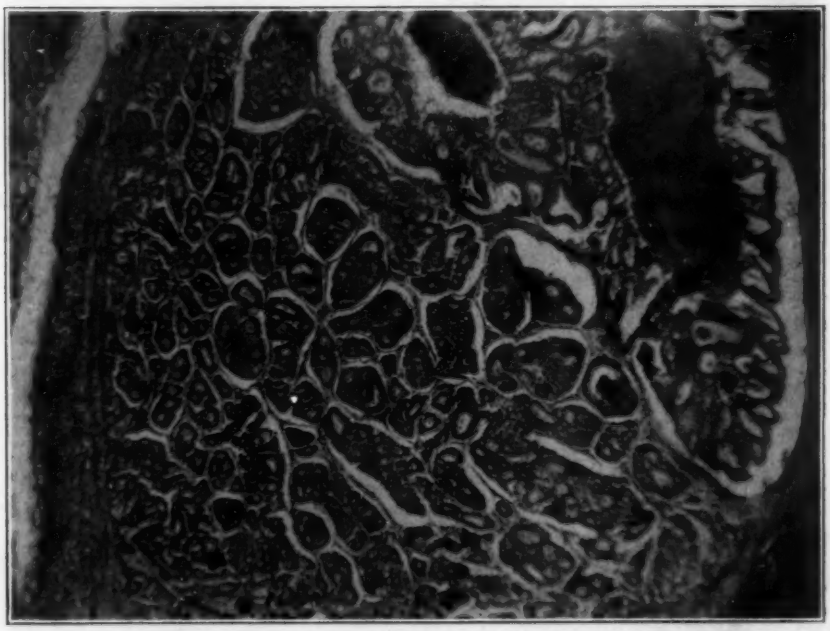

Fig. 11.—Adenoma type of carcinoma, in a patient, aged 88. Duration of condition was one year; patient died two months after operation; acute perforation of gallbladder or duodenum; metastasis? (Slide lent by Bloodgood.)

Influence of Axillary Involvement on End-Result.—Accurate data on this point are available in ninety cases. In twenty-one cases in which the axilla was considered not involved the average survival of the patient after operation was 5.2 years. In sixty-nine cases in which the axilla was involved this average was 2.8 years. Reference to tables 7 and 8 shows that even if the axilla is involved there may be a prolonged survival. Hubbard's patient with axilla involved is alive after thirteen years, Deaver's after seven years. Finney and Bloodgood have had

patients with involvement of the axilla who have died over ten years after operation with recurrence. Finsterer had a patient who died eleven years after operation and who was considered free from cancer.

Influence of Ulceration on End-Result.—Accurate data on this point are available in ninety cases. In forty cases in which ulceration did not occur the average survival of the patient was 4.9 years after operation, and in forty cases in which ulceration occurred the average was 2.4 years. From tables 7 and 8 it would seem that ulceration is more of a factor in connection with prolonged survival than is axillary involvement. In only one case in which ulceration occurred (Bloodgood's) did the patient survive operation ten years, and only seven of these patients have survived five years.

NOTE.—I intend to continue this study of carcinoma in the male breast and would be much indebted if surgeons would furnish reports and slides of other cases whether operation has already been performed, or future cases.

RHABDOMYOSARCOMA OF THE VULVAR ORIFICE IN CHILDREN

REPORT OF A CASE

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The great rarity of tumors of the vagina in little girls and the great pathologic interest attached to such tumors have led me to report a case and to review the literature on the subject.

Tumors of the same histologic structure as the one reported in this article have been found in fishes, in mammals and in man. These tumors have arisen from various parts of the body, e. g., from the uvula, the testes, the ovary, the prostate gland and from the muscle fibers in various portions of the body. This article will be limited to rhabdomyomas of malignant character springing from the vagina. This site seems to be the most common point of origin, with the possible exception of the kidney. Holmes [1] compiled thirty-nine cases in 1906. Other less common sites of origin are the heart, lungs, esophagus and uterus.

Since the report of Holmes on thirty-nine cases, Miller and Gurd [2] have reported a case, of which the following is a synopsis:

REPORT OF CASES

CASE OF MILLER AND GURD.—A girl, aged 2 years and 4 months, had as the first symptoms slight straining during defecation and an offensive vaginal discharge. Vaginal examination under anesthesia revealed a greatly dilated vagina filled with friable, gelatinous tumor masses resembling polypi. Radical operation was performed abdominally, the uterus, appendages and dilated vagina being removed. Improvement was only temporary. The tumor recurred with extension to the abdominal cavity in six weeks, and the child died at the end of two months. Necropsy was not performed.

AUTHOR'S CASE.—*History.*—H. B., a girl, aged 16 months, at the age of 14 months began to pass polypoid masses, the size and shape of muscat grapes, which the mother discovered on the diaper. Up to this time she was a normal child. The tumors increased in number and were frequently accompanied by blood. The child was taken to the family physician who found a large mass of polypi, similar to nasal polypi, springing from the posterior vaginal wall. These were removed but soon recurred. The child suffered severe hemorrhage, causing profound anemia.

The father and mother and two brothers were well.

In February, 1925, she was referred to me for treatment.

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1. Holmes, O. L. Pediatrics **19,** 1907.
2. Miller, C. J., and Gurd, F. B.: Surg. Gynec. Obst. **11**:391-397, 1910.

Physical Examination.—The child was well nourished, but of pasty complexion. The teeth were poor; the throat was normal. The chest, heart, lungs and abdomen were normal. A pedunculated tumor mass, the size of a small orange, which bled easily when irritated, protruded from the vagina. It seemed attached by a rather broad base to the posterior raphe of the vagina. Over its upper surface, many polypoid tumors resembling a cluster of grapes were found (fig. 1). There was a seropurulent, foul smelling discharge.

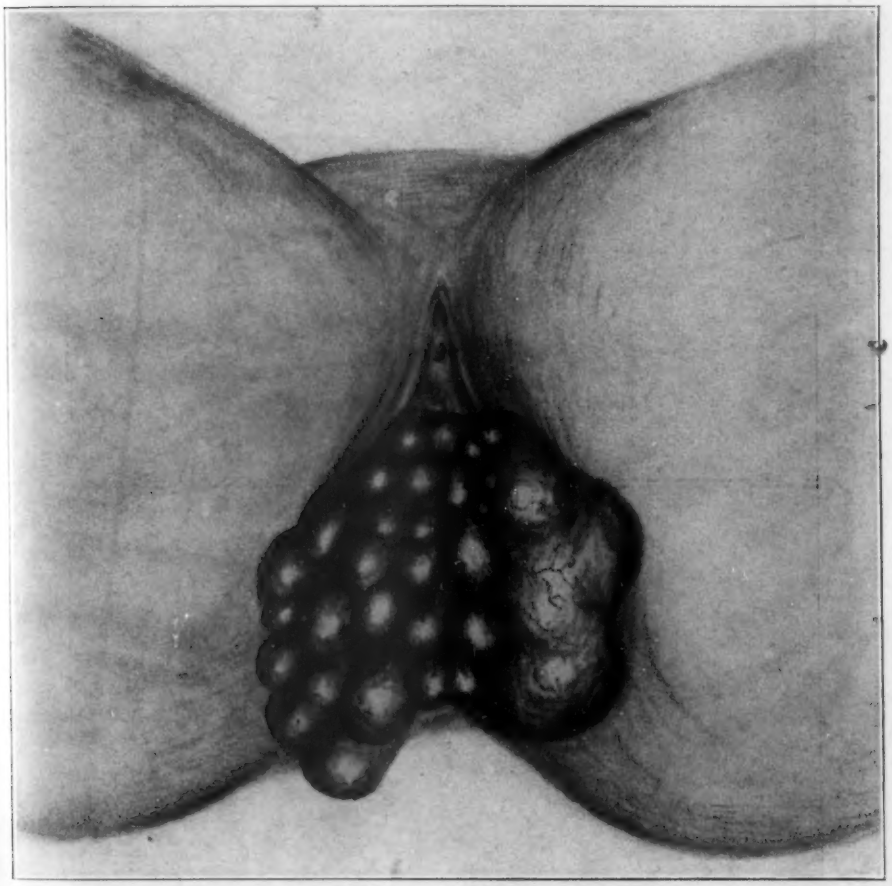

Fig. 1.—Tumor at time of operation.

Treatment.—The tumor was thoroughly removed down to the posterior raphe with the actual cautery. Four hundred milligram hours of radium screened by 2 mm. of lead and 1 mm. of brass was given. The child rapidly regained her health and normal weight.

Pathologic Report.—The removed tumor mass was irregular in shape, 7 cm. long by 5 cm. wide by 2.5 cm. thick, consisting of two parts. One part was made up of dark red pedunculated tumors which in appearance were typical mucous polyps. The largest of these was dark and gangrenous. The main

tumor mass was white and slightly lobulated. One portion on the surface was necrotic. On section the pedunculated tumors resembled a mucous polyp. On section the largest part of the tumor was firm and white, and a clear serum oozed from the cut surface. It was slightly fibrous. Grossly, the diagnosis was multiple polypi springing from a large mass, which, grossly, was a fibromyoma.

The histologic diagnosis was endothelioma, or spindle cell sarcoma (malignant).

Fig. 2.—Appearance of child a few days before death.

The child remained well until Nov. 11, 1925—more than nine months—when she again passed two or three small polypi. These were removed and an additional 300 mg. hours of radium was given. In about two weeks the child began to fail. There was no return of the tumor at the original site, but the abdomen began to fill, and the patient gradually became emaciated. Jan. 27, 1926, the abdomen had become enormously distended; coursing over it were

Fig. 3.—Appearance of child in recumbent position; the distended abdominal veins should be noted.

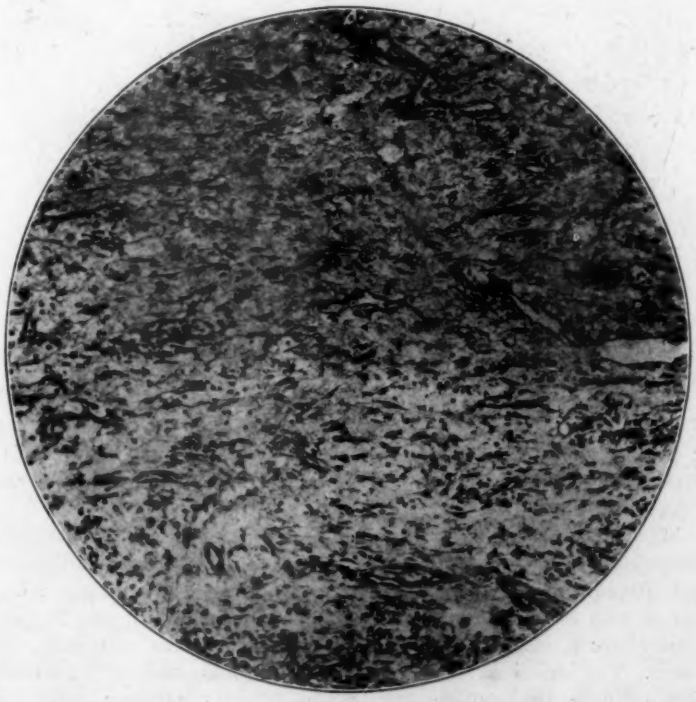

Fig. 4.—Spindle shaped cells, most abundant around blood vessels.

many accessory, distended veins (figs. 2 and 3). The lower part of the abdomen was flat on percussion, and ballottement was present. The upper part of the abdomen was tympanitic. The abdomen was tapped at this time with a large trocar and 100 cc. of bloody fluid evacuated. February 7, one year after my first examination, the baby died of toxemia and exhaustion.

Postmortem Examination.—Dr. B. F. Sturdivant, pathologist to the Pasadena Hospital, reported that the body, that of a small child, was greatly emaciated. The length was 91 cm., and the circumference of the abdomen 78 cm. The ensiform to the navel measured 23 cm., to the pubes 30 cm. There was marked edema of both legs.

The veins of the abdomen had ruptured from pressure. The tumor mass filled the entire abdomen, and had pushed the intestines up high against the diaphragm. The pericardial sac was filled with fluid. Tumor masses were

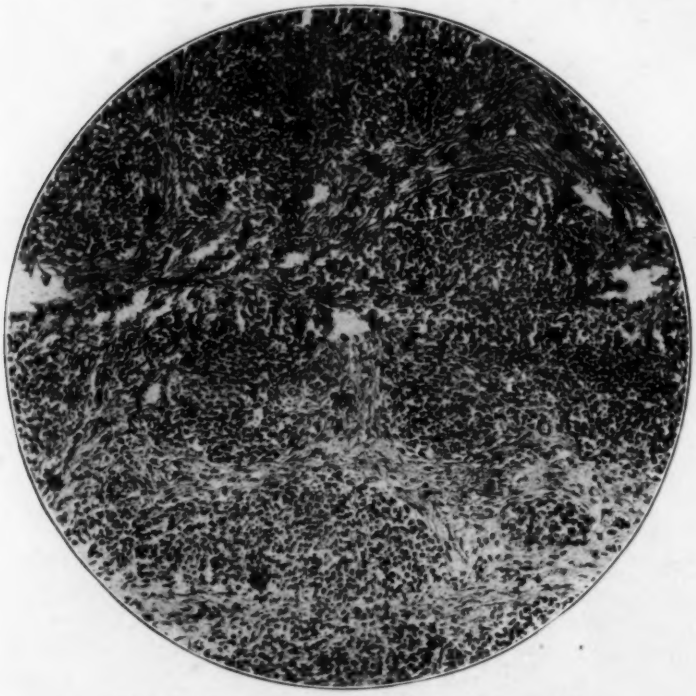

Fig. 5.—Spindle cells forming wide strands.

present on the pericardium. The tumor had broken through the pelvis retroperitoneally, along the vessels. There were many pigmented areas with hemorrhage into them.

The bladder contained a group of tumor masses similar to those in the vagina and in the abdomen. The uterus and vagina were normal. The ovaries were not identified. The liver, gallbladder and spleen were normal. There were one or two tumor masses on the under surface of the diaphragm. The right kidney was dilated and hydronephrotic. There were no tumor masses in the kidneys. The left kidney was normal in size; there was slight dilatation of the pelvis. There were a few tumor masses on the upper surface of the diaphragm, and a few in the retroperitoneal glands. A small tumor mass was

present in the lower lobe of the left lung. The main tumor mass was grayish white and gelatinous.

Microscopic Examination.—The sections showed a soft, edematous tumor, having the appearance of a myxoma. Scattered throughout the tumor, and especially around the blood vessels, were numerous spindle-shaped cells, which made a considerable part of the tumor. In places these spindle cells were gathered together forming wide strands. These spindle cells closely resembled muscle fibers, which showed a great many transitional forms. In some of the sections stained with phosphotungstic acid hematoxylin, a few cells with delicate cross striation could be made out. Longitudinal striation could be easily made out in a number of cells. The tumor was vascular. Rarely, a large cell with a mitotic nucleus was seen (figs. 4, 5 and 6).

The diagnosis was rhabdomyoma (sarcoma botryoides, Pfannenstiel).

Fig. 6.—Cells showing longitudinal and transverse striations.

COMMENT

Tumors of this type have usually been diagnosed as sarcomas. As pointed out by Adami, the whole subject of tumors derived from striated muscle is still involved in uncertainty. Some pathologists, particularly those of the French school, have reported numerous sarcomas which they regard as derived directly from muscle tissue elements, but this view is not generally accepted. The more highly differentiated a tissue, the less liable it is to produce neoplasms. The malignant rhabdomyoma, such as the one reported here, containing imperfectly

developed striated muscle elements, does not spring from fully developed muscle fibers, but arises from embryonic cells which are capable of giving rise to striated muscle in the process of development.

The great malignancy of these tumors would suggest their origin from cells of the embryonic type which have undergone little differentiation. Sarcomas vary in their malignancy in proportion to their amount of connective tissue. Connective tissue tumors in which the cells are capable of producing a large amount of fibrous tissue are less malignant than those in which small spindle cells or round cells predominate. Metastasis is not common in the rhabdomyosarcomas either by the lymphatics or blood stream, but they extend rapidly by continuity. In my case, however, there was metastasis to the lungs.

The literature on this subject shows that these tumors are characterized, first, clinically thus: (*a*) Early symptoms and a period of slow growth, during which there is an apparently benign proliferation of tissue from the vaginal wall, are absent. (*b*) At the vulvar orifice appear tumor masses, polypoid in character, associated with more or less severe hemorrhage, which is often the first symptom and which may vary from a mere stain to copious bleeding. (*c*) Pressure is felt in the bladder and rectum from the growth in the vagina. The tumor may attain a large size and enormously dilate the vagina before appearing at the orifice. The bladder symptoms in my case were so pronounced that the tumor was thought to be a bladder tumor by one of the surgeons who saw it. There was distention of the bladder with incontinence. (*d*) Inflammatory changes appear on the surface of the growth, with sepsis. Urine escaping from the distended bladder seeps into the distended vagina, where it decomposes and sets up an inflammatory process, resulting in a foul smelling, bloody discharge. Owing to the small vulvar orifice, drainage is poor. (*e*) Extension of the tumor takes place by continuity rather than by metastasis. In my case, there was late metastasis to the lungs. The tumor progressed by extension through the vaginal vault into the abdominal cavity. The entire abdomen became enormously distended with polypoid masses. When the diaphragm was reached, the tumor metastasized to the lungs, probably through the blood stream. There was no involvement of the rectum or vagina. The child became greatly emaciated and died of sepsis and inanition.

Second, histologically these tumors are characterized by (*a*) a vascular connective tissue framework, (*b*) imperfectly developed striated muscle—the muscle tissue never attains the full development of mature striated muscle [3]—and (*c*) cells showing transverse striations or

3. Hektoen, Ludvig, and Reisman, David: American Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1901.

beadings. It is generally conceded that these tumors are of embryonic origin. The frequency of their occurrence in infants, their location in regions involved in embryonic infoldings, such as Müller's duct, and the embryonal nature of their essential cells, all point to the reasonableness of this theory.[4]

TREATMENT

These tumors occurring in the genito-urinary tract are almost invariably fatal, there being only one or two reported recoveries. Theoretically, they should be amenable to treatment if recognized early. The local nature of the growth in its incipiency, the rather prolonged period of slow growth and relative benignancy, and the tendency to progress by extension rather than by metastasis, all suggest the possibility of radical cure if the growth is recognized early and treated vigorously. Although she came under observation late and when near death, my patient was restored to perfect health by thorough cautery removal and vigorous radium treatment. If given in the early stages, this method of treatment should offer hope of permanent relief.

4. Hektoen (footnote 3, p. 181).

CIRCUMINJECTION OF AUTOGENOUS BLOOD IN THE TREATMENT OF CARBUNCLES*

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NEW YORK

The purpose of this article is to present the results of the application of a method of defense against the spread of infection in a carbuncle. Carbuncles have been treated by such methods as hyperemia, injection of antiseptics into their centers, ointments, vaccines, roentgen-ray therapy, and conservative and radical surgery, but extensive scarring, lengthy convalescence and the frequency of complicating sepsis or metastatic pus foci accompanying these methods warrant a consideration of any method that may prevent these conditions. To aid healing and to preclude as far as possible the occurrence of septic complications, two factors are essential, first, the least possible trauma to tissue, and, second, the mobilization of the natural forces of defense.

Within the last eighteen years attempts have been made to use whole blood or its constituents locally to combat infection. In 1908, Mueller and Peiser [1] injected the patient's defibrinated blood into nonprogressive pyogenic abscesses. They thought that the proteolytic ferments of the polymorphonuclear leukocytes caused a rapid purulent secretion by digestion. This secretion helped dilute the toxic products and thus delayed their absorption. Lorey,[2] in 1912, used local applications of horse or diphtheria serum in various pyogenic infections complicating diphtheria or scarlet fever. Thus, when a cervical adenitis in scarlet fever was incised and drained with a packing impregnated with horse serum, he said that less sloughing and toxicity resulted and clean granulations appeared early.

Ten years later, in 1922, Rieder [3] sought a method for the treatment of carbuncles and furuncles which would prevent unnecessary injury to tissue and the opening up of new avenues of infection. He observed that if a carbuncle or furuncle was incised crucially without undermining the flaps, the insertion of a packing saturated with horse serum or diphtheria antitoxin made the slough begin to separate in twenty-four hours, and in several days bright red granulations appeared in the bottom

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* From the Presbyterian Hospital and the Columbia University College of Physicians and Surgeons.

1. Mueller, E., and Peiser, A.: Ueber die Technik der Antifermentbehandlung eitriger Prozesse, Beitr. z. klin. Chir. **60**:236, 1908.

2. Lorey: Neue Gesichtspunkte zur Behandlung der Diptherie, des Scharlachs und von eitrigen Prozessen, Med. Klin. **8**:1069 (June 30) 1912.

3. Rieder, Wilhelm: Ueber Behandlung der Staphylomykosen mittels Pferdserums, Klin. Wchnschr. **1**:2333 (Nov. 18) 1922.

of the wound. This result was not obtained by using antiseptics in the same manner. He reported favorable results in sixteen carbuncles and five large furuncles. After the injection of 1 cc. of horse serum into the centers of furuncles, sloughing and healing followed. In 1923, reporting twenty-three cases of carbuncle, some with doubtful prognoses, Rieder [4] called attention to the same treatment, but he was at a loss to explain the rationale, except perhaps that the serum introduced antibodies locally. No anaphylaxis was noticed. In the same year, Laewen,[5] the surgical director at Marburg, discouraged by the death of several patients with fulminating furuncles of the face, injected the patient's freshly aspirated whole blood at the margins of induration of nine furuncles of the face after simple crucial incisions. The infections were progressive rather than fulminating, and the results were favorable. Several months later Laewen [6] described a case of fulminating furuncle of the upper lip in which, after crucial incision, 90 cc. of the patient's unmodified blood was injected just beyond the area of cellulitis. The next day the infiltration and induration were found to be merged. On the third day the temperature and swelling were down. On the sixth day the induration had spread to the other side of the face. Sixty-five cubic centimeters of the patient's blood was then injected as previously. On the ninth day the process had stopped and squeezing did not spread it. Other workers in this field were Nourney,[7] Linhart [8] and Kuhn.[9] Schlesinger,[10] disagreeing with Laewen, preferred excision. He believed that the indeterminate depth of the carbuncle would prevent successful infiltration of blood beneath it.

It occurred to me that circuminjection of autogenous blood in local infections without any operative procedure had some interesting possi-

4. Rieder, Wilhelm: Neue Wege zur Karbunkelbehandlung, Deutsche Ztschr. f. Chir. **77**:300, 1923.

5. Laewen, A.: Ueber die Behandlung fortschreitender pyogener Prozesse im Gesicht mit Inzision und Umspritzung mit Eigenblut, Centralbl. f. Chir. **50**: 1018 (June 30) 1923.

6. Laewen, A.: Zur Behandlung Gesichtsfurunkel mit Inzision und Umspritzung mit Eigenblut, Centralbl. f. Chir. **50**:1468 (Sept. 29) 1923.

7. Nourney: "Ueber die Behandlung fortschreitender pyogener Prozesse im Gesicht mit Inzision und Umspritzung mit Eigenblut" berichtet Centralblatt fuer Chirurgie 1923, nr. 26, die Chirurgishe Klinik in Marburg, Centralbl. f. Chir **50**:1636 (Nov. 3) 1923.

8. Linhart, Walter: Zur Behandlung Maligner Gesichtsfurunkel mit Inzision und Umspritzung mit Eigenblut, Centralbl. f. Chir. **51**:1501 (July 12) 1924.

9. Kuhn, F.: Die Haemorrhagische Behandlung des Furunkels, München. med. Wchnschr. **71**:1432 (Oct.) 1924.

10. Schlesinger, Arthur: Zur Frage der Eigenblutinfiltration, Bemerkungen zu der Arbeit von Laewen in nr. 38 des Centralblattes, Centralbl. f. Chir. **51**: 2583 (Nov. 22) 1924.

bilities and that it would be of value to ascertain whether the spread of infection in a carbuncle could be overcome by this method. If this could be proved in a carbuncle, the use of this therapeutic principle might be of value to check other accessible spreading infections or to minimize the danger of sepsis or purulent metastases. It will be noted that the various authors quoted, in addition to the injection of blood, also incised the carbuncles. No statement is made whether any other aids, such as local heat, antiseptics, ointments or narcotics, were used. Accordingly, it seemed most important to rule out with reasonable certainty the influence of any factors other than autogenous blood circuminjection which might prevent spread of infection, cause sloughing and discharge, alleviate pain and minimize constitutional symptoms. With this in mind, twelve patients who had carbuncles were treated at the Presbyterian Hospital with circuminjection of autogenous blood without other operative procedure under the following conditions:

1. The patients were all nondiabetic.

2. The carbuncles were real and progressive and several colleagues agreed that ordinarily their choice of treatment would be radical surgery. If there was one opinion that a carbuncle might get well with conservative treatment, such as local heat or ointments, that case was not included in the series. In this way at least twenty cases were excluded.

3. Circuminjection of autogenous blood without incision was the only treatment. This method, so far as I know, has not been attempted before.

4. Ambulatory treatment after injection consisted in:

   (*a*) Simple dry dressings.
   (*b*) Abstention from narcotics.
   (*c*) The ordinary measures against constitutional symptoms, such as forcing fluids and limited diet.
   (*d*) Wiping away frank pus, removing separated slough, and keeping the surrounding skin clean.

TECHNIC

The infected area is prepared in the usual manner and the patient anesthetized, preferably with gas and oxygen or ethyl chloride inhalation. The method was tried without anesthesia in two patients who had small carbuncles, but the procedure was too painful. An assistant withdraws blood from the median basilic vein into a 20 cc. syringe. The operator immediately attaches another needle to the syringe and begins the injections just beyond the margin of induration of the carbuncle. The needle is pushed into the skin and an intracutaneous and subcutaneous injection is begun under considerable pressure. Gradually, the needle is pushed perpendicularly deeper and deeper until little pressure is required to force in the blood. At this point the needle has probably penetrated deep enough for the blood to extravasate through the deep necrotic tissue. The needle is then withdrawn. The same procedure is followed until the lesion has been circuminjected, a sterile needle being used for each injection. It is advisable to allow some blood to well up through the center of the carbuncle. The tissues about the carbuncle are seen to swell up because of the injected blood, and a few drops of blood may exude from the punctures. The number of punctures necessary, perhaps from three

to six, varies according to the extent of spread. The amount of blood injected varies with the size of the carbuncle and the amount of induration.

A fairly typical course of a carbuncle of the back of the neck treated in this manner is as follows: Immediately on the patient's recovery from the anesthesia the pain is much diminished and in some cases it has vanished. The patient may be able to turn his head laterally without pain even in cases in which this was not possible before the treatment. The anxious and painful expressions often disappear, also the frequent shooting pains referred to surrounding areas. As a rule, the first good night's sleep is obtained, but it is disturbed if pressure is put on the carbuncle. The patient feels stronger, his appetite is distinctly better, there is an improvement in his mental and physical condition, and he does not feel so feverish. The day after the treatment, pus begins to ooze out of the small openings in the center of the carbuncle and occasionally small sloughs separate. Improvement is rapid, drainage becomes profuse and the indurated and blood injected areas have merged. There is some tenderness at the sites of the injections which gradually disappears; the induration of the injected area may take two weeks to subside. The small openings in the center of the carbuncle coalesce about the third day and bright red granulations begin to appear at the base of the wound. There may be some ecchymosis at the injected area, and the skin within the injected area assumes a violaceous color. Epithelization then gradually takes place, leaving a minimal scar, which in a two year follow-up is found to be superficial, nonadherent, with no induration and in some cases almost invisible.

The cases are described according to a definite scheme, which is self-explanatory, in the accompanying tables.

An analysis of the twelve cases given in the tables follows:

BEFORE INJECTION

I. Age { Oldest, 64 / Youngest, 22 / Average, 46
II. Sex { Males, 11 / Females, 1
III. Location { Back of neck, 11 / Scapular region, 1
IV. Duration before injection { Longest, 21 days / Shortest, 5 days / Average, 10 days — Two had been previously incised
V. Pain { Moderate, 6 / Moderately severe, 1 / Severe, 5
VI. Temperature on admission { Highest, 101 / Lowest, 99 / Average, 99.6
VII. Indurated area { Largest, 9.5 by 7.5 cm. / Smallest, 4 by 4 cm. / Average, 6.1 by 5.4 cm.
VIII. The size of the openings in the center varied from 1 mm. to 3 cm. in diameter.

TABLE 1.—*Data in Case 1*

Before Injection

Age	Sex*	Location	Duration	Amount of Pain	Temperature†	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
22	♂	Back of neck	5 days	Moderate	100.2	7 by 7 cm.	2 by 2 cm.	Moderate	Not done‡	50 cc. at 1, 2, 4, 6 and 8 o'clock§

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area				Time for Complete Closure	Scar
							Tenderness	Induration	Ecchymosis	Violaceous Color		
1	Less on twisting neck; slept 6 hours	99.4	1 slight chill	Present	Moderate; thick yellow slough in center	Less	Moderate	Present	0	0	12 days	Minimal
2	Slight pain on twisting neck to extreme	98.8	0	Slight	3 cc. thick pus; central slough removed	Slight	Very slight	Present	0	Present, 1.5 cm. away from central necrotic area		
3	No pain on twisting neck	98	0	Slight	2 cc. pus and slough; 1 cc. fluid pus expressed	Less	Very slight	Present	0	Present		
4	No pain	98	0	0	0.5 cc. thick yellowish pus; slough 1 cc. in diameter; granulations, bright red	Very slight	0	Beginning to disappear	0	Present		
5	0	97.8	0	0	Few drops; central granulating area 1 cc. in diameter	Very slight	0	Moderate	0	Present		
6	0	97.6	0	0	Slight, serous; pin-sized opening	0	0	0	0	Present		
8	0	98	0	0	0	0	0	0	0	Present		
10	0	98	0	0	Wound practically healed	0	0	0	0	Present		
12	0	97.4	0	0	Wound healed	0	0	0	0	Beginning to disappear		

* In this and the following tables, ♂ indicates male, ♀, female.

† Mouth.

‡ When cultures were not taken, no pus exuded or could be expressed, or there was too much mixed infection, or it was not considered fair to take cultures of the wound after treatment. However, it is known that most carbuncles have Staphylococcus aureus as the infecting agent.

§ Site of injections with reference to numbers on face of clock.

TABLE 2.—*Data in Case 2*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
59	♂	Back of neck	8 days	Slight; slept well; not responding to conservative treatment	99.4	5 by 5 cm.	Many pin-head openings	Moderate	Staphylococcus aureus	40 cc. at 3, 6, 9 and 12 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	0	98.6	0	Slight	2 cc. yellow pus	Slight	Very slight	Slight	0	0	12 days	Minimal
2	0	98.6	0	Very slight	2 cc. pus	0	Slight	Slight	0	Slight		
3	Very slight	98.4	0	Slight; neck can be turned easily	2 cc. pus	0	Slight	Slight	0	Slight	Follow-up, 12 months; scar, 1 by 2 cm.; superficial, not adherent; no induration or depression	
4	0	....	0	0	1 cc. pus	0	0	Slight	0	Slight		
6	0	....	0	0	Small slough expressed	0	0	Very slight	0	Slight		
10	0	0	0	0	0; has oozed out through original openings	0	0	Very slight	0	Slight		
11	Completely healed											

TABLE 3.—*Data in Case 3*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
35	♂	Back of neck	13 days	Severe; agonizing; fever, chills, loss of sleep	99.4	6 by 7 cm.	.....	Severe	Not done	15 cc. at 7, 6 and 4 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Slight; slept most of night	100	0	Slight	Profuse	Present	Present	Present	0	0	15 days	Did not return
2	0	99.4	0	Slight	Profuse	Present	Present	Present	0	0		
3	0	99.2	0	Slight	Profuse	Less	Less	Present	0	0		
4	0	99.2	0	0	Very profuse	Less	Less	Slight	0	0		
5	0	99.6	0	0	Profuse	Less	Less	Slight	0	0		
6	0	99.6	0	0	Profuse	Less	Less	Slight	0	0		
7	0	98	0	0	Less; pus and slough	Less	Less	Slight	0	0		
9	0	98	0	0	0.5 cc.	0	0	Slight	0	Slight		
13	0	....	0	0	Slight; flaps closed	0	0	Slight	0	Slight		

The patient did not return, but treated himself and got well.

TABLE 4.—*Data in Case 4*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
32	♂	Back of neck	6 days	Moderately severe, especially in right shoulder	99.6	8 by 7 cm.; spreading by 4 o'clock	11 small openings over area 3 by 2 cm.	Moderate	Not done	50 cc. at 9, 1, 4, 6 and 7 o'clock

After Injection

							Injected Area					
Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Tenderness	Induration	Ecchymosis	Violaceous Color	Time for Complete Closure	Scar
1	Slept well; turned neck easily; felt well; pain in right shoulder gone	98.8	0	0	2 cc. pus	Merging with blood injection	Practically none	Slight	0	0	13 days	Minimal
2	No pain on twisting neck; felt fine; slept well	97.4	0	0	2 cc. thick yellowish pus; necrotic area 1.5 cm. in diameter	Very slight	0	Slight	0	0	Follow-up, 23 months; scar, 1.5 by 1.5 cm.; extremely superficial, white, cigaret-paper like; not adherent to underlying structures; no induration	
3	None; slept well	98.8	0	Slight	1 cc. thick pus; slough separating; central necrotic area 2 cm. in diameter	0	0	Slight	0	0		
4	None; felt fine	97	0	0	2 cc. pus; 2 small sloughs removed	Merged with blood injection	0	Slight	0	0		
5	0	98	0	0	Slight slough on dressing	0	0	Slight	0	0		
6	0	98	0	0	No more slough; central area 1 cm. in diameter closing in	0	0	Very slight	0	0		
7	0	98	0	0	Slight, serous	0	0	Very slight	0	Violaceous area about granulating area		
8	0	98	0	0	0; granulating area 1 cm. in diameter	0	0	0	0	Present		
9	0	98.8	0	0	Granulations bright red	0	0	0	0	Present, 2 cm.		
10	0	98.2	0	0	0; crusted area 1 cm.	0	0	0	0	Present		
11	0	97.8	0	0	Wound almost healed	0	0	0	0	Present, 2 cm.		
13	0	98	0	0	Wound healed	0	0	0	0	Present, 1.5 cm.		

TABLE 5.—*Data in Case 5*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
52	♀	Scapula region	7 days	Moderate; no sleep 3 nights	100.4	9.5 by 7.5 cm.	2.5 by 2 cm. numerous pustules	Moderate	Not done	70 cc.

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Very slight	99	0	Present	Small amount of thick pus, 1 cc.	Less	Slight	Present	Slight to left	0	39 days	Minimal
2	In axilla	98.6	0	Present	Small amount	7.5 by 7	Slight	Present	Slight to left	0	Follow-up, 24 months; scar, 3.5 by 3 cm., very superficial, loose, cigaret-paper like; not adherent to underlying structures	
3	Very slight; slept well	98.8	0	Present	Small amount; central slough separating	Less	0	Slight	Slight	0		
4	0	99.2	0	0	2 cc. of thick pus	Less	0	Slight	Slight	0		
5	0; movement of arm free	98.6	0	0	Profuse; 2 large sloughs removed	Less	0	Very slight	Circumferential	Marked; 7 by 4 cm. around necrotic area		
6	0	98.6	0	0	3 cc. of thick pus and few large sloughs	0	0	0	Slight	Present		
7	0	98.6	0	0	Pus and slough	0	0	0	Slight	Present		
9	0	98	0	0	Large slough removed	0	0	0	Fading	Present		
10	0	98.4	0	0	Granulations red; wound strapped	0	0	0	Less	Present		
11	0	98.6	0	0	Wound restrapped	0	0	0	Less	Present		
16	0	0	0	0	0; strapped	0	0	0	Slight	Present		
23	0	0	0	0	Strapped	0	0	0	Slight	Present		
30	0	0	0	0	Granulating area, 3 by 2 cm.	0	0	0	Slight	Present		
39	0	0	0	0	Healed	0	0	0	Faint	4 by 2.5 cm.		

TABLE 6.—*Data in Case 6*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
55	♂	Back of neck	3 weeks	Severe; sleepless nights	99	6 by 4 cm.	Pin-head	Slight	Not done	10 cc. at 8, 12 and 4 o'clock (no anesthesia)

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	0; stopped 1 hour after injection	98.8	0	0	Slough separating	Less	Slight	Slight	0	0	21 days	Minimal
2	0	97.5	0	0	2 cc. pus	Less	Slight	Slight	0	0	Follow-up, 24 months; scar, 1 by 0.5 cm.; depressed 2 mm. because in natural crease of neck; not adherent to underlying structures; no induration	
3	0	....	0	0	1 cc. pus	0	Slight	Slight	0	0		
5	0	....	0	0	0.5 cc.	0	0	Slight	0	0		
8	0	0	0	0	1 cc.	0	0	0	0	0		
16	0	0	0	0	Few drops	0	0	0	0	Slight		
21	0	0	0	0	Healed	0	0	0	0	0		

TABLE 7.—*Data in Case 7*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
64	♂	Back of neck	13 days; 3 days before crucial incision; process spreading	Moderate; 3 sleepless nights	100	6 × 5 cm.	2 × 1.5 cm.	Moderate	Not done	60 cc. at 6 points of injection

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	0; slept well; twisted head easily	99.8	0	Slight	2 cc. thick pus; slough liquefying	Moderate	Slight	Slight 6 by 5 cm.	0	0	41 days	Minimal
2	0; twisted head; felt well	100.4	0	Slight	Discharge increasing	Moderate	Slight	Slight 6 by 5 cm.	0	0	Follow-up, 24 months; scar, 6 by 1.5 cm.; extremely superficial, cigaret-paper appearance; not adherent to underlying structures; whiter than surrounding skin	
3	0	99.4	0	Slight	Slough separating; discharge increasing	Less	Slight	Same	0	0		
							Area of lymphangitis spreading toward mastoid					
4	0	99	0	Slight	2 cc. pus; necrotic area larger	Less	0	Slight 6 by 5 cm.	0	0		
5	0	99	0	Slight	More profuse; slough separating	Less	0	Same	0	Present		
									Lymphangitis same			
6	Slight in area of lymphangitis	99.4	0	Slight	Less; slough not separated	Less	0	Less	0	Present		
								Flaxseed poultices for lymphangitis				
7	Slight	99.4	0	0	Slough sticking	Less	0	Less	0	Present		
								Flaxseed poultices for lymphangitis				
8	0	98.8	0	0	Area of necrosis greater; moderate discharge	0	0	Slight	0	Present		
9	0	99	0	0	Slough separating	0	0	Slight	0	Marked		
									Poultices discontinued			
10	0	99	0	0	Slough separating	0	0	0	0	Very marked		
12	0	98.8	0	0	Slough separating	0	0	0	0	Very marked		
15	0	98.8	0	0	Necrotic area 5 by 2 cm.; slough separating	0	0	0	0	Very marked		
18	0	....	0	0	Slough separated	0	0	0	0	Very marked		
21	0	....	0	0	Granulations clean; wound strapped	0	0	0	0	Very marked		
	For next 20 days epithelium gradually closed in; violaceous color persisted											
41	0	0	0	0	Healed	0	0	0	0	Very marked		

TABLE 8.—*Data in Case 8*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
47	♂	Back of neck	One week; incised 3 and 2 days before	Severe; no sleep 3 nights; fever, chills, headache	99.6	4 by 4 cm.	2 by 2 cm.	Marked	Not done	25 cc. at 12, 9, 7, 5 and 3 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Gone 10 minutes after injection. None; slept well; turned neck easily	99.6	0	Slight	1 cc. of thick pus	Slight	Present	Present	0	0	31 days	Minimal
2	None; slept well; turned neck easily	99	0	Slight	1.5 cc. of slough showing	Slight	Present	Present	0	0	Follow-up, 14 months: scar, 0.75 cm. in diameter, superficial; not adherent to underlying structures; thickening in skin and subcutaneous tissue above scar 3 cm. in diameter; no pain or tenderness	
3	0	99.4	0	Slight	Slough, 2 by 1 cm., removed	Slight	Slight	Present	0	0		
4	Some pain	99.2	0	0	2 cc. pus	Slight	Slight	Present	0	0		
5	0	98.8	0	0	2 cc. pus	0	Slight	Present	Slight	0		
6	0	97	0	0	3 cc. pus	0	Slight	Present	Slight	0		
7	0	0	0	0	1 cc. small sloughs	0	Slight	Present	Slight	0		
8	0	0	0	0	Slight	0	0	Present	0	Slight		
9	0	0	0	0	0	0	0	Slight	0	Slight		
14	0	0	0	0	Small granulating area	0	0	Slight	0	Present		
20	0	0	0	0	Healed	0	0	0	0	Slight		

TABLE 9.—*Data in Case 9*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
53	♂	Back of neck	14 days	Moderate; 2 sleepless nights	99.6	5.5 by 6 cm.	2 by 2 cm.	Moderate	Not done	50 cc. at 8, 12, 1 and 2 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Slight; slept 5 hours	99	0	Slight	Profuse thick slough separating	Moderate	Slight	Slight	0	0	32 days	Minimal
2	Slight; slept 6 hours; turned neck easily	99.6	0	0	Profuse; slough separating; area necrosis 3.5 cm. in diameter	Moderate	Slight	Slight; not spreading	0	Present		
3	No pain; slept all night	99.4	0	0	Profuse	Less	0	Slight	0	Present		
4	0	99.2	0	0	Profuse; slough still sticking	Less	0	Slight	0	Present		
5	0	98.2	0	0	Profuse, 5 cc.; 2 pieces slough; area necrosis 2 cm. in diameter	0	0	0	0	Present		
6	0	98.8	0	0	30 cc. pus and slough	0	0	0	0	5.5 by 5.5 cm.		
7	0	99	0	0	Profuse; no slough	0	0	0	0	Present		
8	0	99	0	0	5 cc.	0	0	0	0	Present		
9	0	98.6	0	0	2 cc.; small slough; area necrosis 1.5 cm. in diameter	0	0	0	0	Present		
11	0	98.6	0	0	1 cm. in diameter; small amount pus	0	0	0	0	Present		
13	0	0	0	0	0.5 cc.; granulating area 0.5 cm. in diameter	0	0	0	0	Present		
18	0	0	0	0	0	0	0	0	0	Present		
21	0	0	0	0	Scab	0	0	0	0	6 by 5 cm.		
25	0	0	0	0	Healed	0	0	0	0	6 by 5 cm.		
32	0	0	0	0	.....	0	0	0	0	Present		

TABLE 10.—*Data in Case 10*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
43	♂	Back of neck	6 days	Moderate; lost sleep 5 nights	99.6	5 by 4.5 cm.	Pin-head; 2 openings	Slight	Not done	15 cc. at 7, 12 and 3 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Less; slept 7 hours	99	0	Slight	Few drops	5 by 3 cm.	Slight	Present	0	0	18 days	Minimal
2	0	99	0	Slight	1 cc. pus	3 by 3 cm.	Slight	Present	0	0		
3	0	99.2	0	Very slight	1 cc. pus	3 by 3 cm.	0	Present	0	0		
4	0	98.6	0	0	Profuse	3 by 3 cm.	0	Present	0	0		
8	Follow-up letter stated patient was well. No discharge											
18	0	0	0	0	0	0	0	0	0	0		

TABLE 11.—*Data in Case 11*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
34	♂	Back of neck	6 days	Severe; sleepless night	99	4 by 4 cm.	Several pin-head openings	Moderate	Not done	40 cc. at 1, 2, 6, 8 and 9 o'clock

After Injection

Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Injected Area: Tenderness	Injected Area: Induration	Injected Area: Ecchymosis	Injected Area: Violaceous Color	Time for Complete Closure	Scar
1	Much better; slept well	100.2	0	Increased	Very slight; purulent	Present	Present	Present	0	0	21 days	Minimal
2	Very slight but much less than before injection; slept well; ate whole chicken	99	0	None; turned neck easily	1 cc. pus	Present	Present	Present	0	0	Follow-up, 13 months; scar, 2 by 1 cm.; superficial; not adherent; no induration; no pain or tenderness	
3	None except along glands; appetite fine	99	0	0	2 cc. thick pus	Less	Slight	Slight	0	0		
4	0; felt fine; slept all night	99	0	0	Profuse; 5 cc.	Slight	Very slight	Very slight	0	0		
5	0	98.6	0	0	Very profuse; large slough removed from center of opening 4 by 4 cm.	0	Very slight	Very slight	0	0		
6	0	98.6	0	0	Profuse; no slough; granulations at base red	0	0	Slight	0	0		
7	0	98.6	0	0	Very slight	0	0	0	0	0		
9	0	0	0	0	Very slight	0	0	0	0	Present		
11	0	0	0	0	0	0	0	Very slight	0	Present		
14	0	0	0	0	Very slight; granulating area smooth; 1 cc. in diameter	0	0	0	0	Present		
21	Practically healed											

TABLE 12.—*Data in Case 12*

Before Injection

Age	Sex	Location	Duration	Amount of Pain	Temperature	Size of Indurated Area	Size of Opening	Tenderness	Culture	Amount of Blood Injected
45	♂	Back of neck	9 days	Severe; sleepless 3 nights	101	8 by 6 cm.	3 by 3 cm.	Severe	Staphylococcus aureus	45 cc. at 1, 2, 3, 6 and 8 o'clock

After Injection

							Injected Area			
Day	Pain	Temperature	Chill	Stiffness	Discharge	Induration	Tenderness	Induration	Ecchymosis	Violaceous Color
1	Better; slept better; shooting pains to scalp and ears stopped	100.4	0	Less	Moderate; seropurulent; openings in center larger	Less	Very slight	Present	0	Slight
2	Slept all night; painless; appetite still poor	100	0	Less	2 cc. thick yellowish pus	Less	Slight	Present	0	Increased
3	Greater; did not sleep well; pain radiating forward	100.8	0	Increased	Moderate	Increased	Marked	Present	0	Increased

At this stage, because the process seemed to be spreading, the patient was sent to the hospital. He was treated with flaxseed poultices and the roentgen ray, and was discharged in two weeks without operation. Hospitalization with local heat alone probably would have cured this patient without additional therapy.

IX. Tenderness
- Slight, 3
- Moderate, 6
- Severe, 3

X. Amount of blood injected
- Greatest, 70 cc.
- Smallest, 10 cc.
- Average, 37 cc.

AFTER INJECTION

I. Pain within 24 hours
- None, 4
- Relieved a good deal, 6
- Gone within 1 hour
  - 1 in 10 minutes
  - 1 in 60 minutes

II. Temperature 24 hours after
- Highest, 100.4
- Lowest, 98.6
- Average, 99

III. Chill within 24 hours, none

IV. Stiffness of neck in 24 hours
- Less, 8
- Greater, 1
- None, 3

V. Discharge in 24 hours
- Oozing pus, 8
- Slough, 4

Openings in center larger in all
Pus varied from a few drops to several cubic centimeters
Where there was slough there also was pus

VI. Induration[11] in 24 hours less in all cases.

VII. Injected area

A. Tenderness in 24 hours
- Very slight, 11
- None, 1
- Average time to disappear in 11 cases because one became worse, 4.4 days

B. Induration
- Longest time 21 days
- Shortest time, 5 days
- Average time, 10.1 days in 11 cases; one spread and the patient received other treatment[12]

C. Ecchymosis
- Present, 3
  - 1 appeared in 1 day; persisted 39 days; time of treatment
  - 1 appeared in 5 days
  - 1 appeared in 4 days
- None, 8
- One spread and received other treatment[12]

D. Violaceous color
- Present, 10
- None, 2
- Shortest time for appearance, 2 days
- Longest time for appearance, 16 days
- Average time for appearance, 6 days

VIII. Time for cure (including complete closure) in 11 cases
- Longest, 41 days
- Shortest, 12 days
- Average, 23 days

IX. Scar
- Minimal, 11
- One spread and the patient received other treatment[12]

X. Follow-up, average of 7 cases, 23 months. Recurrence locally of infection, none

Scar
- Adherent to underlying structures, none
- Tenderness, none
- Depression, none
- Induration, slight in 2

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11. Reference is here made to the feel and not the size of the indurated area, as there is a tendency of the indurated and blood injected areas to merge.

12. The infection began to spread three days after circuminjection, and the patient was sent to the ward. He also received roentgen-ray therapy and local heat. The cure in this case cannot therefore be attributed to the injection of blood.

Fig. 1.—Appearance before circuminjection of 60 cc. of autogenous blood; size of indurated area, 6 by 5 cm.

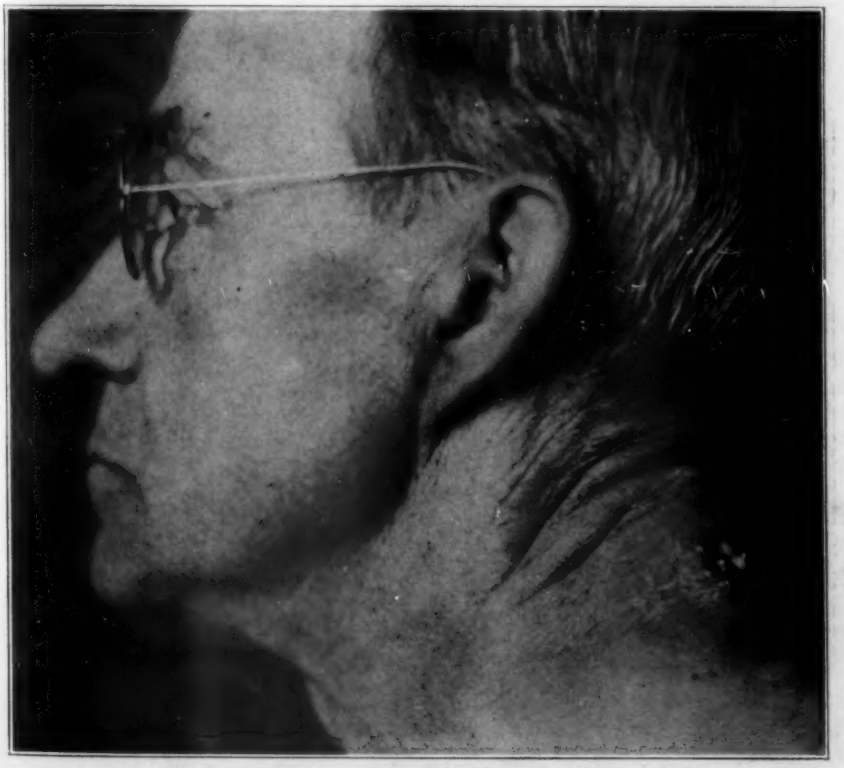

Fig. 2.—Side view of patient shown in figure 1.

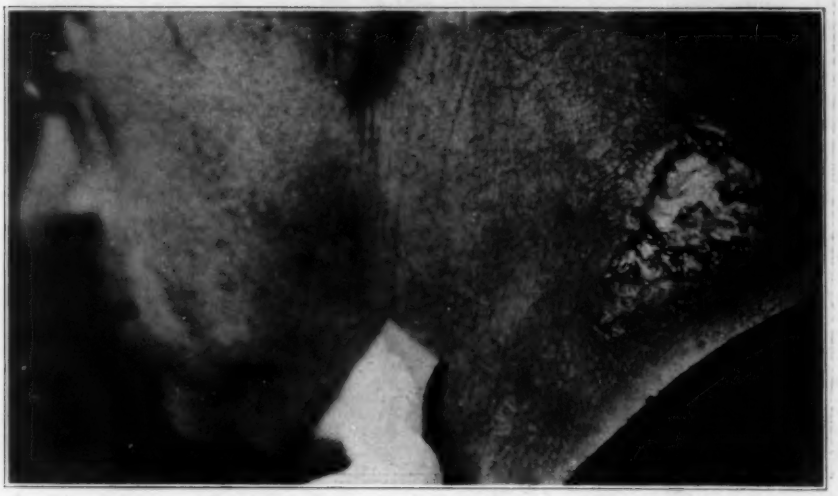

Fig. 3.—Same patient shown in figure 1 ten days after circuminjection, showing extent of lesion, slough and pus.

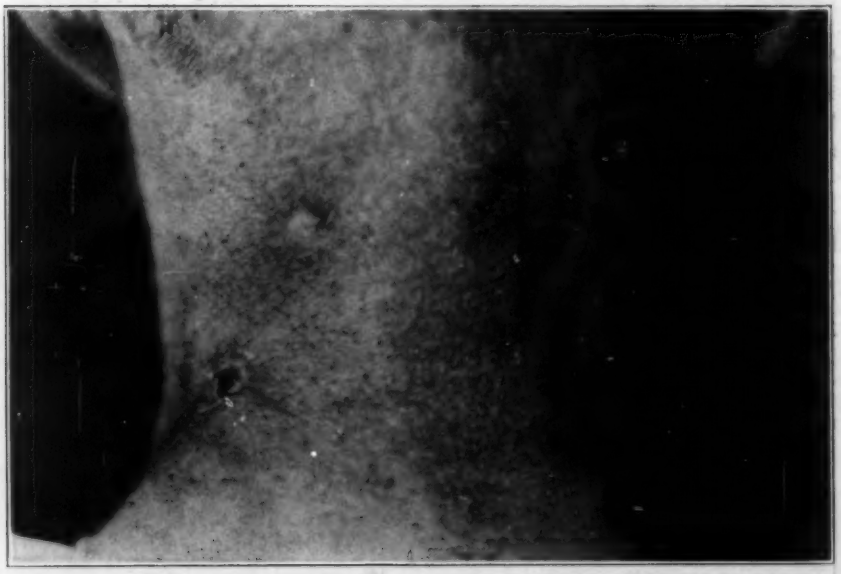

Fig. 4.—Same patient shown in figures 1, 2 and 3 on discharge forty-one days after treatment; the epithelization and absence of marked scarring should be noted.

There are two objections to the method which might be offered. The first is that the injection of the blood might spread infection exactly like a local anesthetic. As a matter of fact, this usually does not happen. Second, the injected blood might become infected. This also did not occur. Apparently freshly injected autoblood behaves differently from extravasated blood which is the result of a trauma. The former produces little injury to tissue. If the blood of an animal is injected into one of its joints or into its pleural cavity, it is quickly absorbed, leaving no permanent adhesions. A traumatic hematoma contains a good deal of serum, and is surrounded by injured tissue, all of which must be either absorbed or extruded. In a traumatic hemarthrosis or hemo-

Fig. 5.—Same patient shown in figures 1, 2, 3 and 4 after twenty-four months' follow-up, showing cigaret paper-like scar, not adherent to underlying structures and not indurated.

thorax, there is slow absorption of the blood, and permanent injury to tissue results. As Laewen [5] expresses it, injection of blood builds a wall against the spread of bacteria while contusion paves a way for it.

SUMMARY

My series includes twelve cases of definite progressive carbuncles occurring in nondiabetic patients. Of these eleven were located on the back of the neck and one in the scapular region. The treatment was ambulatory and, unlike previous methods of therapy, depended solely for its efficacy on circuminjection of autogenous blood without the

utilization of other accessory measures, such as incision, local heat or narcotics. The following results were noted:

The infection did not spread, except in one case.

There was quick relief from pain and constitutional symptoms.

No reaction was observed after injection.

Most of the slough liquefied.

The injected blood seemed to remain in the tissues, with gradual modification, for from several days to two weeks, as evidenced by induration in the injected area, ecchymosis or both.

A violaceous color around the carbuncle appeared in an average time of six days. This might have been an outcome of passive congestion.

I believe that the time for cure was probably shorter than it would have been by surgical procedure, although it would have been impossible to have had a series of exactly the same carbuncles with surgical therapy as a control.

All the patients showed a minimal scar at the time of discharge from the hospital.

In seven of the cases, with an average follow-up of twenty-three months, the scar was superficial, minimal, nonadherent, almost invisible in some instances, and with the negligible induration in two cases.

There was no recurrence of infection locally.

For those who may be interested in the mechanism of the curative phenomena observed in these cases, it might be stated that the increased cellular activity produced by the circuminjection of autogenous blood probably prevents spread of infection and increases autolysis. To elaborate, the following suggestions are offered:

1. *Increase of Local Resistance.*—The injected blood itself produces a powerful positive chemotaxis, so that large numbers of the various leukocytes are mobilized immediately around the infected area. Gay[13] believes that body cells rather than body fluids are the chief factors in the defense processes against micro-organisms. He states that besides polymorphonuclear leukocytes (microphages) the large mononuclear cells of the body (wandering endothelial cells, clasmatocytes of Ranvier, macrophages of Metchnikoff, histiocytes) play a most important part in increasing local resistance. Clasmatocytes, according to Gay, show the following significant properties:

(*a*) When occurring in connective tissue they have pseudopodial processes known as "trailers." In exudates in serous cavities they are usually ovoid in appearance, with a large eccentric and often indented nucleus.

(*b*) Phagocytic power for animal cells, red blood cells, pigment, polymorphonuclear cells and bacteria.

(*c*) Migratory tendencies which are not as marked as in the polymorphonuclear leukocytes but more marked than in the fixed tissue endothelium.

(*d*) Superiority in resisting extraneous influences, which would make them valuable agents in protecting the body against bacteria.

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13. Gay, F. P.: Local or Tissue Immunity, Arch. Path. & Lab. Med. **1**:590 (April) 1926.

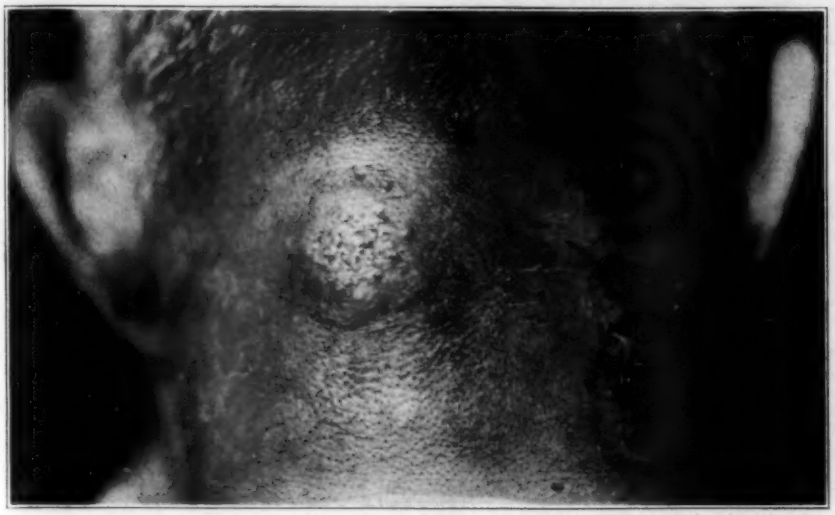

Fig. 6.—Appearance before circuminjection of 40 cc. of autogenous blood; size of indurated area 5 by 5 cm.

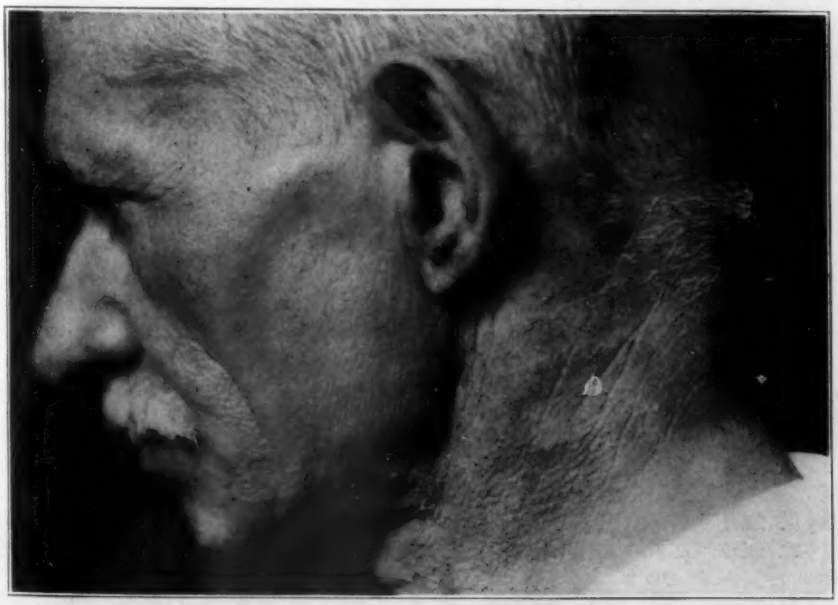

Fig. 7.—Side view of patient shown in figure 6.

Gay[14] and Morrison are firm in their belief that clasmatocytes have a distinct function in the disposal of bacteria, and that they are probably more important than the polymorphonuclear leukocytes in this respect. Gay[15] found that broth, when injected into the simple tissue of the rabbit pleura, produces an increased resistance or active immunity to streptococcus. Granulation tissue forms so that the pleura increases in thickness about forty times. The subserosa is increased in thickness by the infiltration of enormous numbers of mononuclear cells, which, following injections of trypan blue into the cavity, can be shown to be, in significant proportion, true clasmatocytes. Bacteria injected into the pleural cavity are found in an hour or two in the clasmatocytes of the subserous layer under an apparently intact, though modified, serosa which in itself is never phagocytic. In preliminary experiments in pleural immunity, Gay[15] indicates that in advanced grades not only is the original pleura protected but also the other pleura. In this instance, histologically the pleura opposite the immunized one is normal before infection, but on injection of the test dose, protection is acquired by mobilization of previously formed clasmatocytes in the new area. Gay[15] states that he believes that other substances, such as broth, would produce the same action as autogenous blood on a carbuncle. These substances have a tendency to diminish local tissue resistance in the first twenty-four hours, but blood may bridge this gap. Rivers and Tillett[16] corroborate some of Gay's work.

2. *Increased Action of Proteolytic Ferments.*—The greater mobilization of polymorphonuclear leukocytes and clasmatocytes makes this possible. It was clearly noted that the slough in the carbuncles had a tendency to liquefy. Mueller[17] was the first to show that proteolytic enzymes occur in the cells of purulent exudates. Opie[18] demonstrated two proteolytic ferments in leukocytes, which act both in an acid and an alkaline medium but are more efficient in the latter. Bacteria also contain proteolytic ferments.

3. *Introduction of an Antitoxin.*—Following the recent report of Dick and Dick[19] that scarlet fever strains of *Streptococcus hemolyticus* produce a dermatoxic poison for man, Mrs. Parker[20] demonstrated a similar poison in rabbits by injecting sterile filtrates of broth cultures of certain strains of *Staphylococcus aureus.* She also found that small amounts of the serums of many of the rabbits previously injected with filtrates for skin injuring substances easily neutralize

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14. Gay, F. P.: Local Resistance and Local Immunity to Bacteria, Physiol. Rev. **4**:191 (April) 1924.

15. Gay, F. P.: Personal communication to the author.

16. Rivers, T. M., and Tillett, W. S.: Local Passive Immunity in the Skin of Rabbits to Infection with (1) a Filtrable Virus, and (2) Hemolytic Streptococci, J. Exper. Med. **41**:185 (Feb. 1) 1925.

17. Mueller, Friederich, quoted by Kossel: Ztschr. f. klin. med. **13**:149, 1888.

18. Opie, E. R.: Enzymes and Antienzymes of Inflammatory Exudates, J. Exper. Med. **7**:316, 1905; The Enzymes in Phagocytic Cells of Inflammatory Exudates, ibid. **8**:410, 1906; Experimental Pleurisy; the Part Taken by the Enzymes of Leukocytes in the Resolution of a Fibrinous Exudate, Tr. A. Am. Phys. **22**:179, 1907.

19. Dick, G. F., and Dick, G. H.: A Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **82**:265 (Jan. 26) 1924.

20. Parker, Julia T.: The Production of an Exotoxin by Certain Strains of Staphylococcus Aureus, J. Exper. Med. **40**:761 (Dec. 1) 1924.

Fig. 8.—Patient shown in figures 6 and 7 on discharge thirteen days after circuminjection.

Fig. 9.—Patient shown in figures 6, 7 and 8 after twelve months follow-up, showing scar almost invisible, not adherent to underlying structures, and with no induration or depression.

the most powerful staphylococcus poison. Normal rabbit serum, used as a control, had no detoxicating effect, except when incubated with the poison in comparatively large amounts.

In the light of these experiments, one might assume that the circulating antitoxin in the human being, when injected around the soluble toxin producing lesion, might have a beneficial effect on it.

4. *Autohemotherapy.*—Among other observers, Mathieu [21] and Vorschuetz and Tenckhoff [22] have noted a beneficial effect on local infection by the injection of the patient's own blood at a distance from the pus focus.

Laewen [6] believes that the lymphatics around the infected area become blocked by red cells of the injected blood. We have attempted to prove this experimentally in guinea-pigs but have been unsuccessful. Hilgenberg and Thomann [23] found that if poisonous doses of strychnine, curare or cocaine are injected into the tails of mice, more than deadly amounts of the poison can be tolerated if a blood infiltration is performed central to the depot (at the root of the tail). They used fluids of great viscosity, such as blood, serum and gum acacia solution, and found them much better than physiologic sodium chloride solution. Their effect resembled to some extent that of the Esmarch bandage. Laewen also believes that antibodies are introduced locally by the injection of autogenous blood. If present, I believe that their quantity is insignificant.

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21. Mathieu, C.: De l'emploi de la Methode de Descarpentries (sang hemolyse) en Chirurgie, Rev. méd. de l'est **51**:582, 1923.

22. Vorschuetz, J., and Tenckhoff, B.: Von der Behandlung mit Eigenblut, Deutsche Ztschr. f. Chir. **183**:364, 1923.

23. Hilgenberg, F., and Thomann, O.: Experimentelle Untersuchungen über die Aufhebung von Giftresorption durch abriegelnde Bluteinspritzung, Deutsche Ztschr. f. Chir. **180**:267, 1923.

CEREBRAL CONCUSSION *

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The present investigation was begun at the suggestion of Dr. Edward Archibald, in order to determine the physiologic response of the brain to an injury which might conceivably cause coincident concussion and compression. The symptoms of concussion, lasting for some hours, might be masked by and have to be distinguished from, those of an oncoming compression. This idea was suggested by clinical observation of certain patients suffering from severe cranial injury, in whom it was found that death supervened with a blood pressure, a pulse rate and a respiratory rhythm which remained approximately normal until near the end. The hypothesis which, in his conception, might explain such unusual behavior on the part of the vital centers, consisted in the assumption that the well-known opposite effects of concussion and of compression were neutralizing each other; that the raised blood pressure, slowed pulse rate and deepened respiration of compression were brought approximately to normal by the antagonistic concussion effects of low blood pressure, rapid pulse rate and hastened, shallow breathing.

In the original few experiments of this research I aimed at establishing, first of all, the effects of pure concussion in the dog and in the cat as a necessary preliminary to later experiments in which I contemplated the addition of more or less simultaneous compression lesions. This was the more necessary in that there admittedly exists, in spite of a considerable body of experimental work, a great deal of indefiniteness, not to say confusion, in the actual knowledge of concussion, particularly as to its physiology and pathology.

It may be said at the outset that these latter experiments designed to elucidate the original hypothesis have been postponed for the time being, because it soon became obvious that our ideas of concussion itself must be more definite, and there must be a much more general agreement than at present exists. Consequently, the work here recorded represents an attempt at establishing the essential pathologic and physiologic foundation of pure concussion.

Concussion is a clinical term applied to a condition following injury of the head. Originally it was broad in its scope, so broad that Galen [1]

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* From the Department of Physiology and Experimental Medicine, McGill University.

* The expenses of this research were defrayed in part by a grant from James Cooper Fund of McGill University for research in Experimental Medicine.

1. Galen, quoted by Polis, A.: Rev. de chir. **14**:273, 1894.

and Hippocrates [2] and later Ambroise Paré [3] included under the name "commotio cerebri," or concussion, all injuries of the head, even severe cerebral laceration and intracranial hemorrhages. With increasing knowledge, there has been a tendency to limit the term concussion to those cases of injury of the head which do not show the clinical syndrome of cerebral pressure, and to those in which contusion and laceration are not apparent. A fine differentiation between concussion and microscopic contusion is not possible at present because there is no general agreement in the literature as to the exact definition of concussion. It may even be said that the literature is contradictory and confusing. Clinical and experimental investigations have proceeded without beginning on a basis of an exact definition of the meaning of the term concussion or of its scope, and so the literature continues to show many divergent views. It is, therefore, primarily necessary to obtain general agreement as to the exact definition of concussion. A pathologic definition hitherto widely taught is that concussion is part of a condition which has for its pathologic basis scattered microscopic contusions and petechial hemorrhages. On the other hand, the word concussion was originally a purely clinical term. With advancing knowledge, especially knowledge of pathology, and owing to the fact that most cranial injuries ending in death showed certain pathologic changes in the brain, the pathologic definition of concussion just indicated naturally became more acceptable. This, however, was at the expense of physiologic argument, and, as I think, unjustly so; for the essential symptoms of concussion undeniably depend on physiologic disturbances, and it has never been proved that these disturbances are caused by anatomic lesions, such as scattered microscopic contusions. Therefore, a clinical physiologic definition should be accepted. The term concussion should be used to indicate a group of symptoms which are the result of a temporary inhibition of cortical function, with or without stimulation or inhibition of one or more of the medullary centers, but which are not accompanied by pathologic lesions.

The conclusion is widely accepted among surgeons that the essentials of concussion are an immediate loss of consciousness, with or without symptoms suggesting medullary effects, and with a progressive tendency toward recovery; further, that pure concussion, that is, concussion without gross lesion, can cause immediate death. If this clinical definition is accepted, the physiologic phenomena and the symptoms may be correlated by means of animal experimentation. The information obtained from hospital cases is naturally somewhat restricted. In the

2. Adams, F.: The Genuine Works of Hippocrates, New York, William Wood & Company **1**:254.

3. Paré, A.: Oeuvres complètes d'Ambroise Paré, éd. Malgaigne, Paris, J.-B. Baillière **2**:23, 1840.

patients who die of injury of the head, autopsy practically always shows numerous contusions and petechial hemorrhages in the brain. The majority of investigators have concluded that concussion and contusion are synonymous. Rare cases, however, have been reported in which postmortem examination did not show any gross lesion. Such deaths occur almost instantaneously at the moment of the accident. When death occurs later, autopsy always shows lesions caused by contusion. If the foregoing restricted definition of concussion is accepted, the latter cases must be considered as cases of concussion plus contusion. It is consequently unnecessary to endeavor to analyze the symptoms of a mixed condition of concussion and contusion in a study of concussion. The symptoms of concussion are immediate and generalized; those of contusion, progressive and tending to localization. Such a conception eliminates a great deal of the pathologic and physiologic research which has been made concerning concussion, as this research has been based on an investigation of both concussion and contusion. Nevertheless, I shall review this work, as such a review will show the need of a general agreement concerning the definition, and will also be useful later in showing that the term concussion should be limited to designate the condition which is the immediate result of an injury of the head from which the patient gradually recovers or which results in immediate death. Working on this fundamental conception, I shall offer evidence to explain the etiology of concussion, its relation to the symptoms resulting from the effects on the medullary centers, and the relation of concussion to contusion.

SYMPTOMS OF CONCUSSION

Concussion is always caused by an impact on the head, resulting in immediate unconsciousness. Light blows on the head often cause transient vertigo, grogginess, "sparks before the eyes" and similar symptoms but such a condition is of little clinical interest and appears to be largely the result of a mechanical stimulation applied to the central nervous system by means of the blow. Immediate unconsciousness is generally accepted as the constant symptom in concussion. The symptoms of concussion are mainly referable to the cortex, to the medullary centers and to a certain degree to the proprioceptor system, especially the labyrinth. It is presumably the stimulation of the labyrinth which results in the vertigo following the transient unconsciousness. The cortical symptom is the immediate, generalized paralysis of the psychic areas, while the medullary symptom depends on the severity of the blow, and is either stimulation or inhibition of the bulbar centers, which causes changes in the blood pressure, pulse rate and respiratory rhythm.

Cases of concussion are rarely seen by a trained observer from the moment of onset. Gussenbauer's [4] classic case has not this disadvantage

4. Gussenbauer, quoted by Archibald, E.: Am. Pract. Surg., ed. by J. D. Bryant and H. Buck, New York, William Wood & Company **5**:147, 1908.

and will be taken as a typical example of severe concussion. The following account is taken from Dr. Archibald's monograph on surgical affections of the head.

> Gussenbauer and a friend, while on a tour through the Alps, suffered a fall down the Eiger. The friend was rendered unconscious. Gussenbauer fortunately came to no harm. On rising, he found his friend completely unconscious; the pupils were wide; the corneal and other reflexes were abolished; all the muscles were flaccid; the face was deathly pale; and a chance wound was not bleeding. He was not breathing and looked quite lifeless. Evidently, there was both cardiac and respiratory standstill. After a short while, there returned, spontaneously, signs of life; first the pulse, very weak and slow; then the respiration, shallow and slow; then bleeding from the wound. Later, the reflexes appeared; the man gradually began to hear; half opened his eyes; and returned to a condition of semi-consciousness. After a while he fell into a sleep that lasted twenty-four hours; and it was only then that he acquired full consciousness. A week later, all concussion symptoms had disappeared, save that he had lost all memory of the events immediately preceding the accident.

While this example shows the severe type of concussion, most cases are comparatively mild, and there is almost immediate and complete recovery. Probably the best examples of such mild cases are to be found in the boxing ring; these concussions are caused by what is generally known as "the knock out blow." As a result of a sudden blow, usually on the chin, there occurs a sudden loss of consciousness, with flaccid paralysis. The fighter has ten seconds in which to recover sufficiently to get on to his feet and renew the fight, when he may go on to victory. It is inconceivable that such cases are accompanied by any gross lesion, just as it would appear doubtful that Gussenbauer's case was accompanied by a solution of continuity in the central nervous system sufficient to cause such generalized effects. Unless confined within narrow limits to the silent areas, which even then would not be sufficient to cause unconsciousness, gross lesion would give symptoms prolonged over a considerable period. Neurons destroyed in the brain tissue are not repaired but replaced by fibrous connective tissue. This suggests strongly that sequelae are due to gross lesions. Thus the clinical symptoms suggest the limitation of the word concussion to those cases which do not show any gross lesions. Retrograde amnesia may be an exception, but it is unknown whether this is functional or due to an organic lesion.

As all injuries of the head, whether concussion, contusion or hemorrhage, are caused by violence it is obvious that all three must often be present simultaneously, especially in severe cases. Such cases frequently lead to confusion in diagnosis and treatment. In cases of concussion, however, there is either spontaneous recovery or immediate death, so that this diagnosis can be eliminated in those cases in which the course is protracted. Cerebral pressure gives a typical syndrome, with raised

blood pressure and slowed pulse rate. If this conception is accepted, the differential diagnosis of injury of the head becomes comparatively simple, and the factors concerned in the causation of symptoms can be analyzed.

RELATION OF CONCUSSION TO CONTUSION

A review of the literature dealing with the question of the relationship of concussion and contusion shows a great divergence of opinion. Further experimental evidence is required to settle the question as to whether concussion can occur without accompanying gross lesions. Experimental evidence will be given later to support this view.

Boirel,[5] in 1677, was the first to suggest that some cases of injury of the brain were so transient that accompanying lesions of the brain could be excluded. This opinion found marked support in the observations made at an autopsy performed by Littré [6] on a young man who died instantaneously on throwing himself, head first, against a prison wall. Littré did not find any microscopic contusions nor intracranial hemorrhages. Others, Sabatier,[7] and Boyn,[8] and Mourier [9] gave similar negative reports. The diagnosis of concussion thus became limited to those cases which did not show any gross lesions. A reversal of opinion soon occurred, when more careful microscopic observations on the part of better trained men persistently revealed the finer lesions of contusions. Ferrari,[10] working in Kocher's laboratory, showed that in the flinging movement of the brain in response to severe blows on the head, the soft brain struck the bony covering with sufficient force to break small glass ampules buried in the brain tissue at a depth of 5 mm. Kocher,[11] on this evidence, concluded that concussion and contusion were synonymous. Fano [12] considered the symptoms in injury of the head due to contusion, not to concussion. Alquié [13] wrote "la commotio comme lésion differant essentiellement de la contusion est une invention imaginaire." Pirogoff [14] and Beck [15] always found gross

5. Boirel: Traité des plaies de tête, 1677.

6. Littre Acad. roy. de sc. de Paris, 1705, p. 54; quoted by Polis, A.: Rev. de chir. **14**:274, 1894.

7. Sabatier: Med. Operat. **2**:400; quoted by Miles, A.: Brain **15**:154, 1892.

8. Boyn: Thèses de Paris, no. 4, 1818.

9. Mourier: Thèses de Paris, no. 119, 1834.

10. Ferrari, reported by Kocher, in Nothnagel: Spezielle Pathologie und Therapie. Hirnerschütterung, Vienna, Alfred Hölder, 1901, p. 320.

11. Kocher, T., in Nothnagel: Spezielle Pathologie und Therapie, Hirnerschütterung, Vienna, Alfred Hölder, 1901, p. 267.

12. Fano: Mém. sur la commot. du cerveau, Mém. Soc. de chir. **3**:163, 1853; quoted by Polis, A.: Rev. de chir. **141**:278, 1894.

13. Alquié: Gaz. méd. de Paris, 1865, pp. 226, 254, 314, 382, 396, 463, 500.

14. Pirogoff, quoted by von Bergmann: Deutsche Chirurgie, 1880, p. 296; and by Trendelenburg: Deutsche. med. Wchnschr. **36**:1, 1910. Pirogoff: Grundzüge der allgemeinen Kriegschirurgie, Leipzig, p. 77, 1864.

15. Beck, B.: Virchows Arch. f. path. Anat. **75**:207, 1879.

due to hyperacute compression of the brain as the cause of the symptoms of concussion."

Cannon [32] found further support for this hypothesis in his demonstration that the initial rise of intracranial pressure, due to a blow causing inbending of the skull, was sufficient to prevent blood entering the cranial cavity. It is well known that cerebral anemia leads to paralytic symptoms similar to those of concussion. Hill [35] produced unconsciousness and spasm in animals by ligating the four arteries to the head, confirming the results of Kussmaul and Tenner,[36] who produced immediate loss of consciousness and voluntary movement by ligating the innominate artery and the left subclavian. Convulsions occurred in from 10 to 45 seconds. The unconsciousness and the flaccid paralysis seen in syncopal attacks are usually ascribed to cerebral anemia.

In a thorough experimental investigation of concussion, Polis [37] found that he could produce concussion more readily if he first ligated one or more of the arteries to the brain. He finally concluded that cerebral anemia alone would cause concussion, and that concussion was the result of two factors—cerebral anemia and "ébranlement" or molecular disturbance. Kocher,[11] Kramer,[38] Cannon [32] and others, after experimental investigation, supported the hypothesis that cerebral anemia is the sole cause of concussion.

Fischer,[39] and later Miles,[40] thought that the cerebral anemia was due to reflex contraction of the blood vessels owing to the sudden movements of the cerebrospinal fluid following the blow, which was assumed to stimulate the restiform bodies. In the light of present knowledge concerning the vasomotor supply of cerebral vessels, this theory must be abandoned.

Witkowski [41] produced a condition similar to concussion in the frog after removal of the heart. Cerebral anemia could hardly be a factor under these circumstances. Though the evidence supporting the theory that cerebral anemia is the direct cause of concussion appears to be comparatively conclusive, several investigators, Tilman,[42] Rahm,[43] Bres-

35. Hill, L.: The Cerebral Circulation, London, 1896.

36. Küssmaul and Tenner, quoted by Hill, L.: The Cerebral Circulation, London, 1896.

37. Polis, A.: Rev. de chir. **14**:274 and 645, 1894.

38. Kramer, S. P.: Ann. Surg. **23**:163, 1896.

39. Fischer, H.: Volkmann, Samml. klin. Vortr. se. 1 **27**:219, 1871.

40. Miles, A.: Brain **15**:153, 1892.

41. Witkowski, L.: Virchows Arch. f. path. Anat. **69**:498, 1877.

42. Tilmann: Arch. f. klin. Chir. **59**:236, 1899.

43. Rahm, H.: Zentralbl. f. Chir. **47**:146 (Jan.-June) 1920.

lauer,[44] Duret,[45] Koch and Filehne[23] arrived at very different conclusions.

For instance, the opposite conclusions of Koch and Filehne[23] are most striking. They produced concussion by means of repeated light blows in place of the single severe blows used by most other investigators. Repeated light blows would not alter the conformation of the skull to a degree sufficient to cause cerebral anemia, but might, through summation of effect, cause an effect on the central nervous system similar to that caused by a single severe blow. These investigators concluded that concussion was the result of molecular disturbance or "ébranlement." Bergmann[25] supported these conclusions, and the hypothesis received considerable popularity. By molecular disturbance they evidently meant that concussion was due to a direct mechanical effect on the structural equilibrium of the cells.

Brief mention must be made of Duret's[45] theory of cerebrospinal shock as the cause of concussion. Duret forced fluid into the lateral ventricles to reproduce the sequence of events in the skull following the appearance of the zone of indentation caused by a blow. This lessening of the volume of the skull raises the intracranial pressure so that the cerebrospinal fluid in the ventricles is forced violently through the aqueduct of Sylvius. It then is supposed to impinge on the floor of the fourth ventricle, and to cause the minute contusions and petechial hemorrhages so often found in the region of the aqueduct in persons dying from the results of injury of the head. Duret produced similar lesions in his experiments, and considered these lesions as the pathologic basis of concussion. The paralytic symptoms of concussion were due to reflex anemia, the wave of cerebral spinal fluid stimulating the restiform bodies which caused reflex contraction of the intracranial blood vessels. Miles,[40] after a series of experiments of a similar nature, later supported Duret's work. He considered, further, that the scattered petechial hemorrhages so often found in persons dying of concussion were due to pressure changes on the arterioles caused by this sudden rush of cerebrospinal fluid. This produced rupture of the thin-walled vessels. As opposed to this theory, Tilanus and Deucher[46] were able to produce experimental concussion after aspirating the cerebrospinal fluid. Kocher[11] later demonstrated lesions in a patient who had not suffered a primary loss of consciousness similar to those described by Duret. These experiments, together with the difficulty of considering the results of a blow causing concussion as similar to the increase of intracranial pressure produced by Duret, have led to the abandoning of his hypo-

44. Breslauer: Beitr. z. klin. Chir. **121**:590, 1921.

45. Duret: Arch. de physiol., 1874, p. 320; quoted by Tilmann: Arch. f. klin. Chir. **59**:239, 1899.

46. Deucher: Deutsche Ztschr. f. Chir. **35**:145.

thesis. That reflex cerebral anemia of any generalized extent does not occur, has already been stated.

The recent work of Breslauer [44] is not well known. Breslauer found that he could not produce unconsciousness by manual pressure on the cerebrum in dogs, for only when the medulla was involved did unconsciousness occur. He concludes that concussion is due to purely medullary effects. All physiologic evidence, however, tends to place the seat of consciousness in the cortex, and mild cases of concussion show scarcely any stimulation or inhibition of the medullary centers, so that it is difficult to accept Breslauer's reasoning.

A different and interesting line of thought was followed by Tilman,[42] who ascribed concussion to the tearing apart of the white and gray matter. As the white and gray substance of the brain have different specific gravities, they attain different degrees of acceleration in the induced field of gravity set up by an impact on the head. The tendency is for them to be torn apart, the resulting solution of continuity causing unconsciousness. The prompt recovery in most cases of concussion makes this hypothesis untenable. Rahm,[43] however, applies this line of reasoning to the cell particles forming nervous tissue. Protoplasm is an emulsion containing, among other things, lipoids, large protein molecules and electrolytes suspended in a watery base. These particles, having different specific gravities, take up new positions relatively in response to the new gravitational field set up by the violent movement of the brain in toto (Felizet) which invariably follows a severe impact. Until these particles resume a normal equilibrium in the earth's gravitational field, the cells cannot function. Thus the generalized paralytic conditions seen in concussion are explained. This is purely hypothetic, but is apparently in accord with physical possibilities. Examination of the active cells, vitally stained, shows the particles of the protoplasm in constant movement. This, however, does not altogether rule out the possibility of Rahm's hypothesis being correct to a certain degree.

Trendelenburg [47] denied that concussion is caused by anemia, suggesting that the unconsciousness is caused by a physiologic loss of function of nerve cells, which corresponds closely to that produced by narcosis. I would suggest, however, that narcosis is invariably due to a chemical agent, usually a lipoid solvent, which apparently reverses the polarity of the synapse (Bayliss [48]) replacing excitation by inhibition. It is difficult to give sound physicochemical reasons for an analogy between narcosis and concussion. The one is a chemical effect on the synapsis first, the other purely mechanical.

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47. Trendelenburg, F.: Deutsches med. Wchnschr. **36**:1, 1910.

48. Bayliss, W. M.: Principles of General Physiology, London, Longmans, Green & Company, p. 427, 1920.

MEDULLARY EFFECTS IN CONCUSSION

The confusion concerning the physiologic and pathologic basis of concussion is thus evident. Careful examination of the experimental methods adopted by past investigators in the study of concussion shows that in most cases a general anesthetic has been used. This obscures the predominant symptom of concussion, namely that of immediate and complete unconsciousness. Further, cats, dogs and rabbits have been used for most experiments. As these animals, belonging to a much lower order in the scale of evolution than man, depend to a much greater degree on spinal reflexes, the results of injury of the head might correspondingly be different. Again, most investigators have carefully recorded the blood pressure, the pulse rate and the respiratory rhythm, noting the changes produced by blows on the head, and have drawn conclusions from them. The vast majority of mild cases, however, show very slight if any medullary effects while the severe cases show an immediate arrest of respiration with stimulation of the vagus and vasomotor centers. In the present investigation many of the experiments of previous workers were repeated, but it soon became evident that little could be gained from such methods. To cause medullary effects, the blows are necessarily sufficiently severe to cause coincident contusion and hemorrhage. The medullary effects produced are those of stimulation or inhibition of the bulbar centers. Thus any agency which will stimulate or inhibit these centers, produces changes similar to those produced by blows on the head. The onset of concussion consequently cannot be judged from changes in the blood pressure, the pulse rate or the respiratory rhythm.

EXPERIMENTAL INVESTIGATION OF MEDULLARY EFFECTS UNDER VARYING CONDITIONS

In the following experiments, the work of several previous investigators was repeated in order to judge the value of blood pressure changes and alterations in the respiration and pulse rate in the demonstration of the physiologic and pathologic changes in varying types of injury of the head. Dogs and cats were used and were anesthetized with either ether or amytal. The respiratory rhythm was recorded through a tube inserted in the trachea, one of the arms of which connected with a writing lever resting on a tambour. The blood pressure was recorded in the usual manner by connecting a cannula placed in the carotid to a mercury manometer, on one arm of which floated the writing pointer. Comparison was made of the medullary effects produced by the following agencies.

1. Blows on the head.
   (*a*) Single severe one.
   (*b*) Repeated light taps.

2. Electrical current on the medulla oblongata.
   (*a*) A weak induction current.
   (*b*) Galvanic current of 120 volts.
3. Direct mechanical pressure on the medulla oblongata.
4. Cerebral anemia.

The striking similarity in the alterations in blood pressure curve and respiratory rhythm produced by these different means readily shows the impossibility of demonstrating the etiology of concussion by these methods.

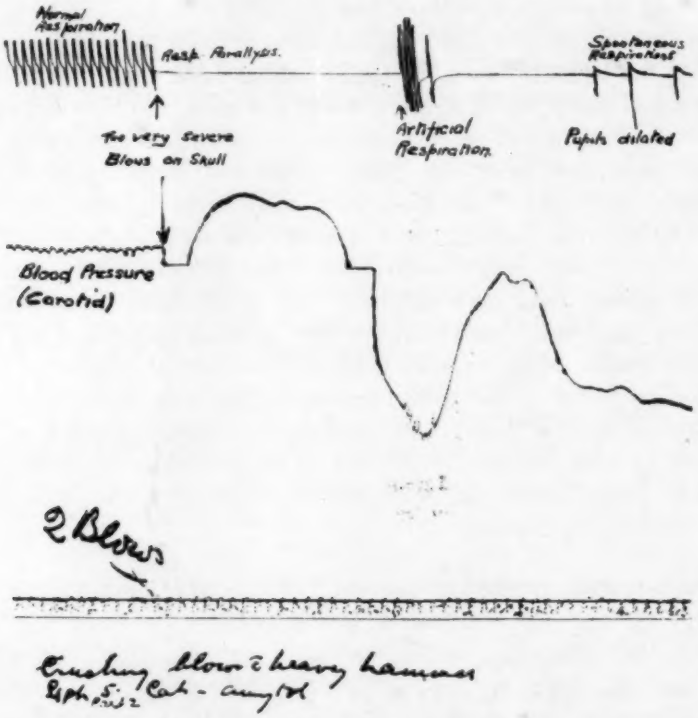

Fig. 1.—Respiratory and blood pressure changes following a severe blow on the head of a cat. Note arrest of respiration with an immediate fall in blood pressure, followed by a rise.

EXPERIMENT 1.—*Effect of severe blows on the head.*

A well nourished cat was used for this experiment. The first blow was delivered on the head with a wooden mallet weighing 175 Gm. The blow was moderately severe but did not produce any marked changes in blood pressure, although a slight rise was evident with a deep respiratory effort. Two severe blows were now inflicted on the head of the same animal with a metal mallet weighing 400 Gm. Respiration immediately stopped, with a sudden fall of blood pressure and arrest of the heart action. The blood pressure changes after the recovery of the immediate fall shown in figure 1 are essentially those following arrest of respiration in asphyxia.

EXPERIMENT 2.—*Effect of repeated light blows on the head of animals.*

This experiment was based on those of Koch and Filehne. Dogs were used under amytal anesthesia. The repeated light blows, inflicted with a light wooden mallet produced marked stimulation of the bulbar centers as seen in the deep, rapid respirations and rising blood pressure. There was also slowing of the pulse rate, evidently due to stimulation of the vagus center. When these blows were continued over a long period, respiratory paralysis finally occurred. With the arrest of respiration, the pulse rate and blood pressure curve (figs. 3 and 4) followed changes almost similar to those noted in the previous experiment (fig. 1) although there was not the marked initial rise in the blood pressure. This was evidently due to the fact that the vasomotor center had been stimulated by the

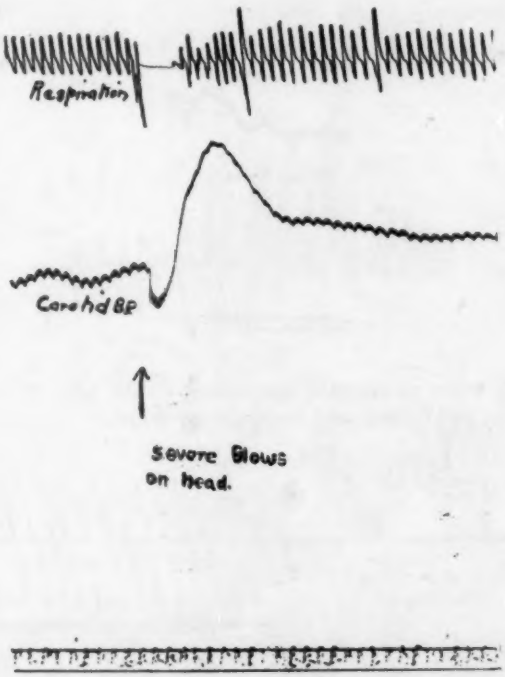

Fig. 2.—Respiratory and blood pressure changes following a severe blow on the head of a cat.

blows from the outset of the experiment, and was not capable of further stimulation by the increasing H-ion concentration resulting from this secondary asphyxiation.

EXPERIMENT 3.—*Effect of electrical stimulation of the medulla.*

A dog was used under amytal anesthesia in this experiment. The medulla was exposed by removal of the atlanto-occipital ligament. Stimulation of the medulla with a weak induction current produced marked stimulation of the respiratory center with a fall of blood pressure soon followed by a rise (fig. 5). When a current of 120 volts was allowed to flow through the medulla there was an immediate fall of blood pressure followed by a brief rise which soon fell to zero. Analysis of this curve (figs. 6 and 7) again shows a similarity to that produced in asphyxia.

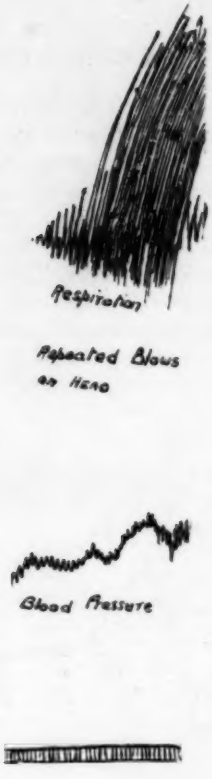

Fig. 3.—Early effect of repeated light blows on the head of a dog. Note the stimulation of the respiratory and vasomotor centers.

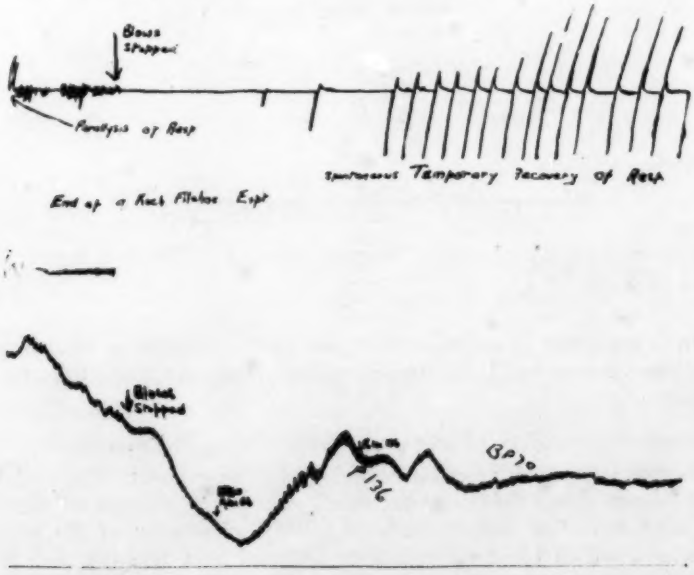

Fig. 4.—End of experiment shown in figure 2. Note that the respiratory center is temporarily paralyzed. The blood pressure rapidly falls, probably due to exhaustion of the vasomotor center.

EXPERIMENT 4.—*Effect of weight falling on the dura.* (Modified experiments of Maassland and Saltikoff.)

A large dog was used under ether anesthesia. Two holes were trephined in the skull, one on either side. Into one was screwed, in air-tight fashion, an instrument for recording the rise in intracranial pressure. The rubber membrane over the end of the inner tube rested directly on the brain. The other end of the tube was connected with a piston recorder. A long brass tube was screwed into the other hole, protected from resting on the dura by a brass flange. The dura on this side was not incised. A known weight could thus be allowed to fall down this tube on to the dura from any height, and the effects on the intracranial pressure were noted. When a weight of 350 Gm. was allowed to fall from a height of 6 inches, respiratory and vasomotor stimulation occurred (fig. 8). There was an immediate slowing of the pulse rate due to vagus stimulation. When

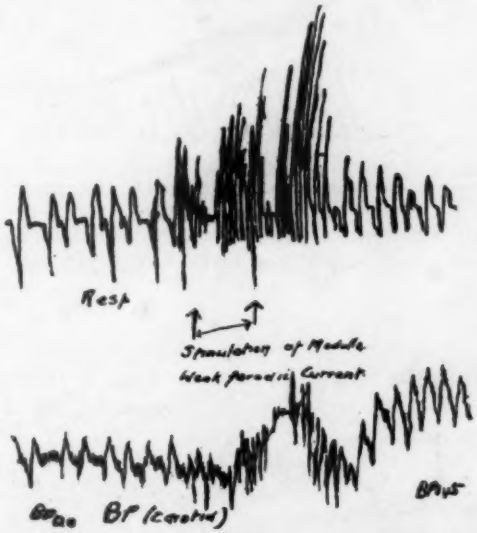

Fig. 5.—Effect of a weak induction current on the medulla. Note the marked stimulation of the bulbar centers.

the weight was allowed to drop from a height of 27 inches, there was immediate cessation of respiration, with a blood pressure curve again similar to that of asphyxia when the blood pressure had recovered from the immediate fall which occurred (fig. 9). The intracranial pressure showed an immediate rise and fall due to the movement of the brain (fig. 10). There soon followed a gradual rise, as shown by Cannon, which he ascribed to the edema resulting from the trauma to the brain tissue, though it may be in part due to resulting small hemorrhages.

EXPERIMENT 5.—*Direct mechanical effects on the medullary centers.*

Dogs were used under ether anesthesia. The mechanical effects were produced by injecting saline solution into the cisterna magna. When 10 cc. of physiologic sodium chloride at 37 C. were injected, marked stimulation of the bulbar centers occurred (fig. 11). When 12 cc. of this solution was forcibly injected in a similar manner, immediate paralysis of the respiratory center occurred. There was, first, a slight fall of blood pressure, soon followed by changes similar to those produced in asphxia (fig. 12).

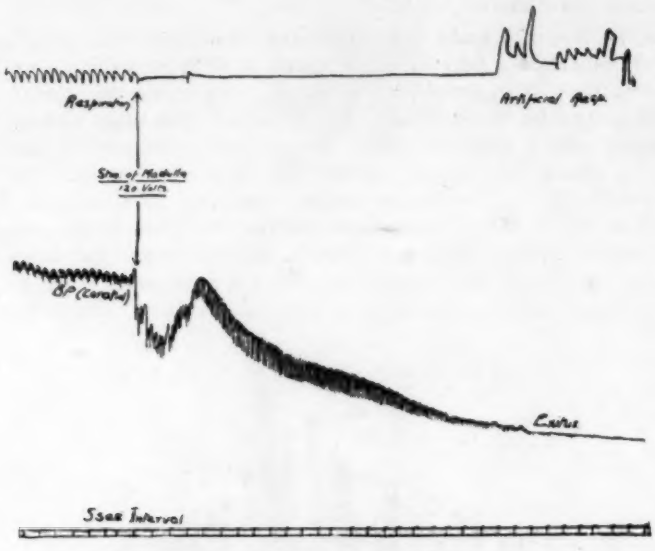

Fig. 6.—Effect of a current of 120 volts on the medulla. Note the immediate paralysis of respiration with stimulation of the vagus and vasomotor centers.

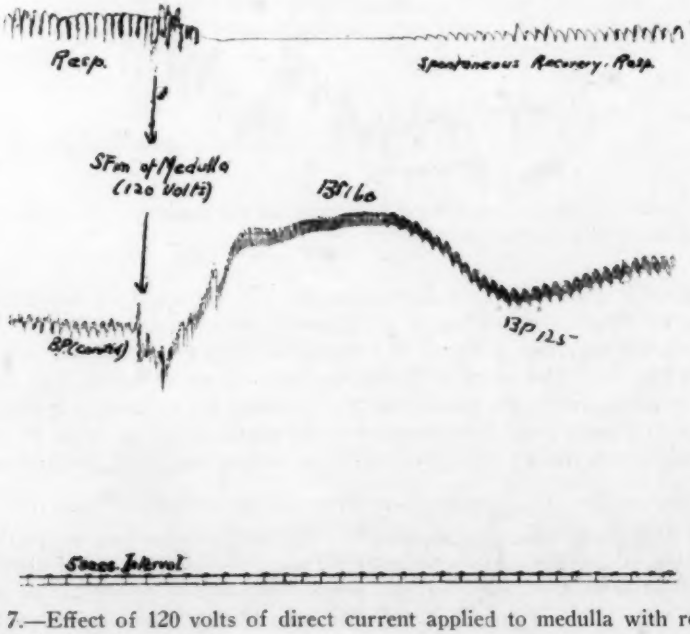

Fig. 7.—Effect of 120 volts of direct current applied to medulla with recovery of respiration.

Fig. 8.—Effect of a weight of 350 Gm. falling on the dura from a height of 6 inches. Note the respiratory and vasomotor centers show stimulation.

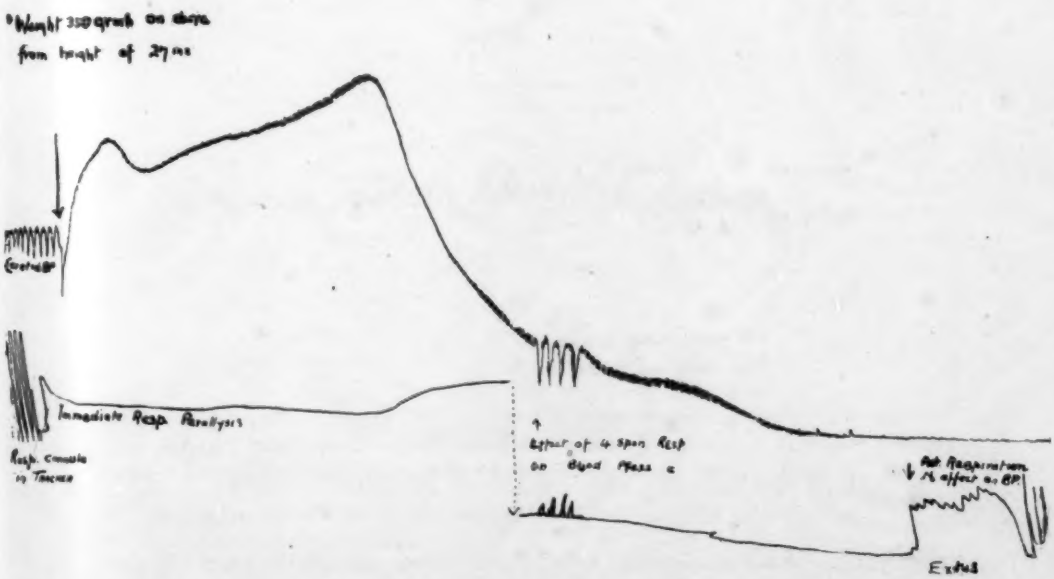

Fig. 9.—Effect of a weight of 350 Gm. falling on the dura from a height of 27 inches. Note immediate respiratory paralysis with a fall in blood pressure followed by a sharp rise, then a second slow fall to zero.

The striking similarity of these results is readily apparent if they are compared with similar tracings showing the effects of complete cerebral anemia (fig. 13) and of asphyxiation (fig. 14).

These tracings appear to show that the marked blood pressure changes produced when respiratory arrest is caused by any means are due to asphyxiation. The respiratory center is always the first to be

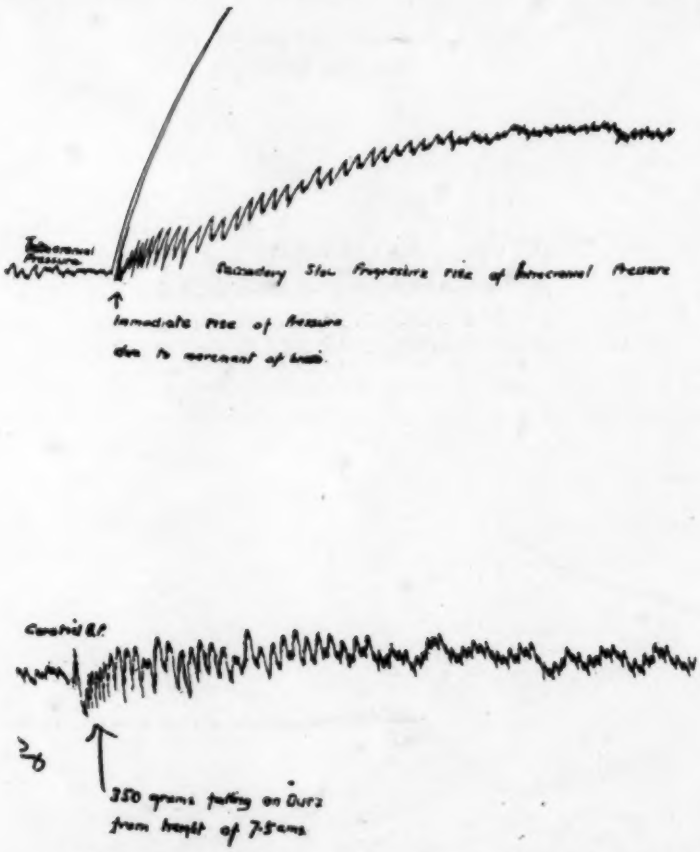

Fig. 10.—Effect on the intracranial pressure of 350 Gm. falling on the dura from a height of 3 inches. Note the immediate rise of intracranial pressure due to the movement of the brain, also the gradual rise due to the resulting edema (Cannon [28]).

paralyzed. With mechanical effects not severe enough to paralyze the respiratory center, a marked stimulation of respiratory movements occurs; further, there is an immediate fall of blood pressure, shown by Kocher [11] to be due to vagus stimulation. He pointed out that this fall did not occur when the vagus had been sectioned previously. This sudden fall soon gives way to a rise of blood pressure, due to early

vagus escape when the stimulation of the vasomotor center becomes apparent. The results are the same whether the agency affecting the medulla is mechanical, electrical or nutritional. Cushing has shown that cerebral anemia produces stimulation of the vagus and vasomotor centers. All these agencies stimulate when of moderate degree. Stimulation, however, changes to inhibition, or paralysis, if the external agency is too severe. First, the respiratory center is paralyzed and a

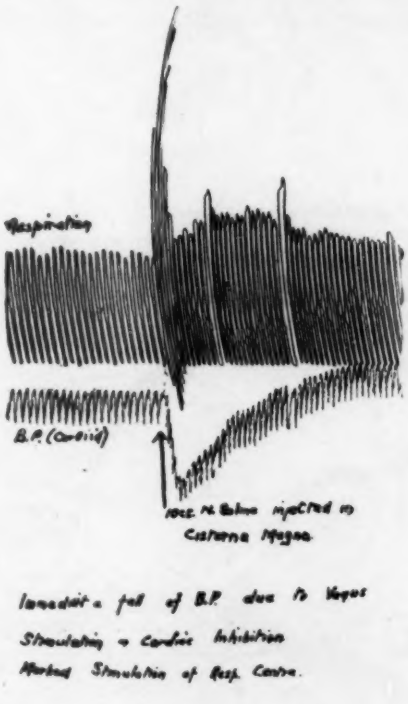

Fig. 11.—Effect of 10 cc. of physiologic sodium chloride injected into the cisterna magna. Note the immediate fall of blood pressure followed by a rise, also the respiratory stimulation.

condition of asphyxia exists. Maassland and Saltikoff were able to paralyze the vagus and vasomotor centers, together with the respiratory center, by placing heavy weights on the dura. This seems possible, though this effect has not been obtained in any of the numerous experiments carried out in the present research. The vasomotor center would appear to have an extraordinary resistance to violence.

The conclusion drawn from these results is that a mechanical effect, such as concussion appears to be, if of a moderate degree, will stimulate the medullary centers, but if of sufficient severity will tend to paralyze them. Von Bergmann has stated that mild degrees of concussion are always accompanied by a slower pulse rate and a rise of blood pressure with a somewhat greater respiratory effort, which is evidently a mechanical stimulation of the centers concerned. Ferrari has shown that in the movement of the brain following an impact on the head there is considerable mechanical violence to the brain. Gussenbauer's case, cited above,

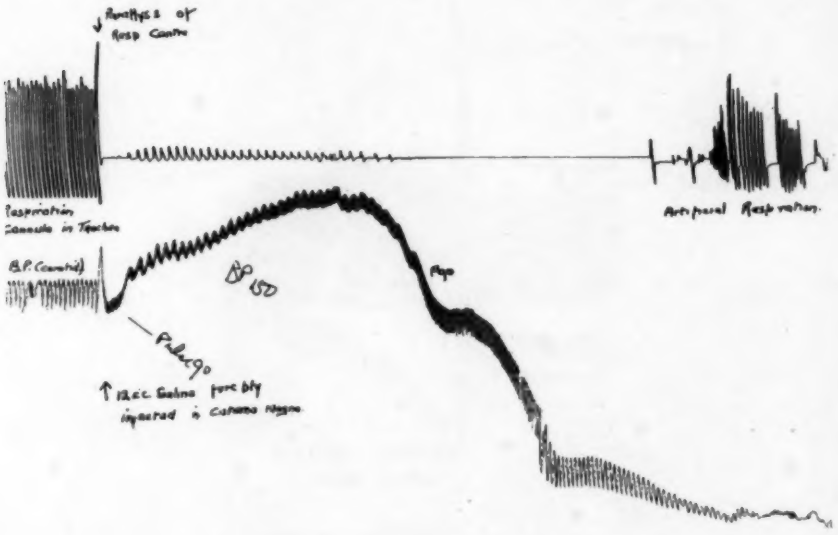

Fig. 12.—Effect of 12 cc. of physiologic sodium chloride forcibly injected into the cisterna magna. Note the similarity of the blood pressure changes to those in asphyxia.

exemplifies this mechanical effect of a sufficient severity to paralyze the respiratory center temporarily. The arrest of the heart was evidently due to vagus stimulation inhibiting the heart action. Thus mechanical violence alone could readily produce the symptoms seen in concussion. Cerebral anemia acts in precisely the same manner; moderate anemia stimulates the medullary centers, while severe anemia paralyzes the respiratory center. Study of the blood pressure and respiratory changes, therefore, will never assist in explaining the place of anemia in the causation of concussion. As there is experimental evidence that anemia

Fig. 13.—The effect of complete cerebral anemia on the respiratory, vasomotor, and vagus centers. (From Hill: Cerebral Circulation.)

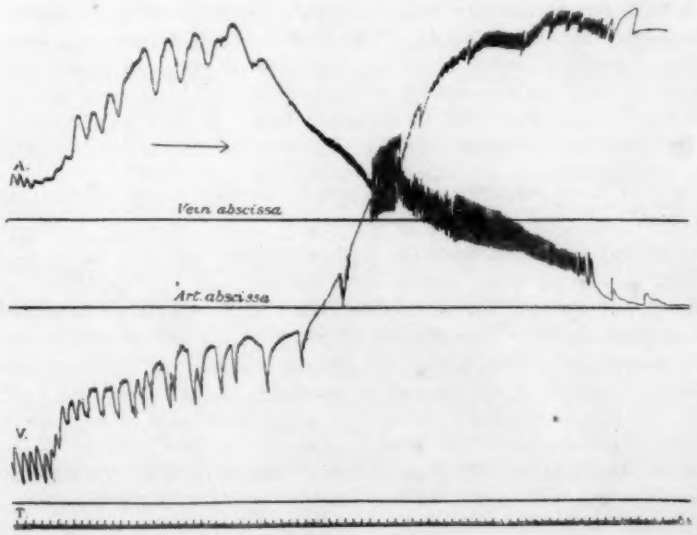

Fig. 14.—Effect of asphyxiation on blood pressure; when the venous pressure curve crosses the arterial pressure curve the pulse pressure increases, and the blood pressure remains constant for a few moments. This also occurs with respiratory paralysis, produced by blows, electricity currents and mechanical pressure. (From Halliburton: Textbook of Physiology.)

may have a place in the causation of concussion (Cannon, Felizet), and as it is generally recognized that cerebral anemia will produce paralytic conditions similar to those occurring in concussion, it is necessary to show conclusively whether sudden anemia will or will not produce immediate unconsciousness. The inbending area of the elastic skull following a blow which forces out the fluids from the skull will immediately spring out again. Any anemia, therefore, must be exceedingly transient, certainly less than one second in duration. It seems improbable that an anemia of such a short duration could cause such widespread paralytic symptoms. All the cells of the central nervous tissue are not adjacent to capillaries, and these cells could hardly be affected by such a transient anemia. Further, it has never been demonstrated, and seems very unlikely, that in the frequent cases of the "knock out" blows the indirect force of the blow on the base of the skull can cause a sufficient diminution in the size of the cranial cavity to squeeze out the fluid contents. It, therefore seems, *a priori,* very unlikely that cerebral anemia is the cause of concussion. The following experiments give considerable support to this contention.

CEREBRAL ANEMIA PROBABLY NOT CAUSE OF CONCUSSION

EXPERIMENT 1.—*Concussion in the heartless frog.*

The heart is removed from a frog under light general anesthesia. On recovery from the anesthesia the frog appears to be conscious. If it receives a sharp blow on the head, a condition arises which appears to be analogous to concussion. The frog lies on its back, without moving and all reflexes are lost. In a few moments it recovers and rights itself and all reflexes return. A blow on the head of the normal frog produces a similar condition analogous to that of concussion in man.

EXPERIMENT 2.—*Complete cerebral anemia in the rabbit without loss of consciousness.*

Under a local anesthetic (procaine hydrochloride), the sternum is opened in the midline, care being taken not to open the pleura. The ascending aorta is dissected out, and clamped for periods of from 1 to 7 seconds. It is evident that this will produce an immediate anemia of much longer duration than that produced in concussion. The animal in this case does not lose consciousness. Immediately on putting it on its feet, it struggles and gives all signs of being conscious. Trapping experience shows that when rabbits are given a sharp blow on the head they immediately lose consciousness for several seconds. Concussion can therefore readily be produced in rabbits by means of blows on the head, but not by transient cerebral anemia of five seconds' duration.

These experiments show that in both the frog and the rabbit, though a condition exactly simulating concussion can be produced readily, it is not the result of cerebral anemia. A transient cerebral anemia even of five seconds' duration does not produce unconsciousness. It is evident, then, that these experiments confirm the arguments stated above, that cerebral anemia is not the cause of concussion. In early experiments

dealing with the effect of immediate cerebral anemia produced by ligating the carotid and vertebral arteries, it is probable that the four arteries were not ligated simultaneously, but that the operation lasted a few seconds. Thus the impression was gained that cerebral anemia causes immediate unconsciousness (Hill [35]).

THE RELATION OF CONCUSSION TO MICROSCOPIC CONTUSION

I have already stated that a great controversy appears in the literature on the question of the relation of concussion to multiple contusions and petechial hemorrhages, many considering the conditions synonymous. If the conclusions reached previously are accepted, it is evident that a mechanical force paralyzing cell function need not necessarily be associated with cell death. It is evident that the generalized, transient, cortical paralysis seen in concussion is not the result of cell death, otherwise prompt recovery could not occur. Following contusion or petechial hemorrhage, an inflammatory reaction and repair process necessarily follow. The immediate symptoms would not, as in concussion, be the most severe, but rather the later symptoms would appear gradually with the development of reactionary edema and further cell death. The lesions would tend to cause a prolonged rise of the intracranial pressure; adjacent tissues would suffer from the edema, and so a protracted course with increasing severity of symptoms might be expected; further, destroyed neurons would not be replaced, but removed, and the lesion would be repaired with fibrous connective tissue. Thus sequelae of a more or less permanent character would result, unless the contusions were restricted to the silent areas. But prompt and complete recovery is generally accepted as one of the outstanding characteristics of concussion. Concussion and contusion can hardly be synonymous, as stated by Kocher.

Concussion can cause temporary paralysis of the respiratory center with prompt recovery. There could be no recovery if this damage were due to a contusion of the respiratory center. Contusion is synonymous with cell death. If the temporary paralysis of the respiratory center in concussion is prolonged beyond narrow limits death will occur. Thus death can occur in pure concussion. This explains why Kramer and Horsley,[38] and later Cannon,[32] by means of artificial respiration, resuscitated animals in which the respiratory center had been paralyzed by blows on the head.

Death, however, rarely occurs in cases of concussion without the added injury of numerous contusions and petechial hemorrhages. The medulla is well protected from injury by its position and only severe violence will cause immediate, prolonged, paralysis of the respiratory center. Ferrari showed how readily contusion of the cerebrum resulted from violence to the head. In response to the blow, the soft brain is

thrown against the bony covering on the opposite side (contre coup). With the narrowing of the diameter of the skull caused by the zone of indentation, the brain may be nipped between the two sides of the cranium. It is possible that, as Duret suggested, the spinal fluid is forced down the narrow aqueduct of Sylvius, causing the lesions so frequently found in patients dying from injuries of the head. Thus it is that cases of injury of the head rarely come to autopsy without showing some gross lesion of the brain. Theoretically, however, concussion alone can kill, when death due to respiratory paralysis will be practically immediate, that is, will occur during the first ten minutes. Deaths occurring after the lapse of some hours are due to contusion, hemorrhages or the results accruing from these, such as edema.

Experimentally, however, it has never been demonstrated that concussion can be produced in animals without the accompaniment of gross lesion. The following experiments were devised in order to support the arguments advanced above. Trypan blue injected intravenously stains all the tissues, except those of the central nervous tissue, a deep blue. Should there be any inflammatory reaction of the central nervous tissue, or any gross lesion, that area will also take on the deep blue stain. This would appear a useful method of showing distinctly whether concussion can be produced without the presence of a gross lesion.

EXPERIMENT 1.—Two rabbits were used for this experiment. The first one was given general ether anesthesia. After trephining the skull, a fine needle was inserted into the cortex, the operation being conducted with aseptic surgical technic. A normal rabbit was then given a blow on the head of sufficient severity to cause unconsciousness of short duration. The blow was dealt with an instrument made by filling a thick rubber tube with lead shot, as such an instrument would be less likely to cause hemorrhages and contusions. The unconsciousness was presumed to be a condition analogous to concussion in man. In rabbits recovery from concussion is rapid. Within a minute the animals move about naturally and take food just as before. On each of the following three days, 20 cc. of a 1 per cent solution of trypan blue in physiologic sodium chloride was injected intravenously. On the fifth day the rabbits were killed and the brains hardened in situ by the injection of 50 cc. of a 10 per cent formaldehyde solution into the carotid artery. After forty-eight hours, the brains were removed and examined. In the rabbit in which the needle had pierced the cortex, a deep blue area in the cortex showed clearly where the needle had entered. This was surrounded by an area of pale blue to which, apparently, the inflammatory reaction had extended. The brain of the animal which had received the blow on the head, was without the stained area, neither were there any hemorrhages present, either subdural or scattered through the brain.

These experiments were repeated several times. Wherever the brain was damaged, the damaged area took up the stain and was colored a deep blue. The brains of animals which had suffered from concussion did not take the stain. Some of these animals showed subdural hemorrhages,

but they were not constant in position or degree and could not have been influential in the onset of the generalized cortical paralysis seen during concussion. These experiments demonstrate that concussion and contusion are not synonymous.

COMMENT

It was stated at the beginning of this article that it would be limited to an endeavor to establish the fundamental physiologic and pathologic basis of concussion. The main factors of confusion appear to lie in the difficulty of clearly differentiating concussion from lesions involving definite histologic and anatomic changes. Without general agreement or a definition of concussion, its scope and etiology, further work would appear futile. It has been shown, both by argument and experiment, that the term concussion should be used to denote the generalized, paralytic effects of an impact on the cortex and medulla, and should be distinguished from the term contusion, whether a gross or microscopic contusion is meant, and also from the term hemorrhage, whether reference is made to a diffuse or petechial hemorrhage. On the other hand, the term contusion should be limited to designate those cases in which destruction of cells can be assumed, and in which there is a tendency toward prolongation or aggravation of symptoms. It has been shown further that mechanical force, a stimulant when of small degree, can act like any other external factor, and paralyze cell function if of sufficient severity. The widely accepted hypothesis that cerebral anemia is the cause of cerebral concussion has been disproved by experiment and by argument. If the blood pressure tracing of complete cerebral anemia is compared with that of cessation of respiration by blows, it is seen that in the former the blood pressure rises immediately while the respiratory center shows deep respirations for seven or eight breaths (fig. 11). The paralysis of respiration due to a severe blow on the head is instantaneous, and there is a sharp drop in blood pressure due to vagus arrest of the heart (fig. 1). This evidence alone would cast doubt on the suggestion that concussion is due solely to cerebral anemia. The effects of concussion are immediate, while the paralyzing effects of cerebral anemia are not immediate but develop after five or more seconds. Thus it appears that concussion is the direct result of a sudden mechanical force on the central nervous tissue, which perhaps is the same conclusion at which Koch and Filehne arrived when they suggested that concussion was due to molecular disturbances or "ébranlement."

To endeavor to understand by what mechanism mechanical force can paralyze cell function, is to enter the realm of speculation. It is known that an electrical current which can produce a similar result, disturbs the equilibrium of the charged particles. The positively charged ions, for example, will be attracted toward the negative pole. The effect of a

mild current is stimulating, that of severe ones, paralytic. A mechanical force, suddenly changing the pressures about the cells, may also disturb the equilibrium. The activity of cells depends on the equilibrium of the physicochemical state of the cells and of their environment.

The sudden violence with its rapid increase of pressure and quickly changing gravitational field might conceivably disturb this equilibrium and so cause temporary loss of function. Rahm has suggested that in response to the new gravitational field, the equilibrium of particles of different specific gravity will be disturbed. With this temporary disturbance of the physicochemical and gravitational equilibrium a loss of cell function might occur which, being generalized over the whole cerebrum, would cause the transient unconsciousness so typical of concussion. The medulla, being well protected by its position, would be saved from the greater part of this disturbance, and so paralysis of the medullary centers would be rare, as is actually the case.

Thus concussion readily lends itself to an etiologic explanation on purely mechanical grounds. Cerebral anemia is not involved. Contusions, though also mechanically produced, represent a more advanced lesion in that actual cell death is caused. Thus concussion is an immediate, transient, loss of consciousness with or without cell death, caused by the direct action of mechanical violence on the cells of the brain, and with no direct causative relations to cerebral anemia. It is distinct and separate from contusion or hemorrhages, whether minute or large and diffuse.

CONCLUSIONS

1. Concussion is immediate in onset, and tends to spontaneous recovery without sequelae.

2. Concussion must be sharply differentiated from all gross lesions, such as contusion and multiple petechial hemorrhages.

3. The most important symptom of concussion is complete unconsciousness with or without medullary symptoms.

4. Cerebral anemia is not a factor in the causation of concussion.

5. Concussion appears to be due to direct mechanical action on the cells which causes a disturbance of cell equilibrium and temporary loss of function.

6. The medullary effects are those of stimulation or paralysis of the respiratory, vagus and vasomotor centers.

7. The respiratory center is the first to be paralyzed. As this is usually a temporary paralysis, artificial respiration may save life.

8. Death from concussion is immediate and is due to respiratory paralysis with consequent asphyxia.

CONGENITAL ATRESIA OF THE ESOPHAGUS

WITH ESOPHAGEAL DIVERTICULUM AND TRACHEO-ESOPHAGEAL FISTULA

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The first case report found in the literature according to McClellan and Elterich,[1] was cited by Thomas[2] and dated in 1696. Plass[3] reviewed the literature in 1917, and found 204 cases up to that year Reynolds and Morrison[4] placed the total number of cases at 214 in 1921. In 1922, Steffen[5] and Willard[6] each reported another example of the anomaly. McClellan and Elterich[1] added another case in 1923. A diligent search of the literature reveals only one case since that time—a recent case reported by Flood.[7] This case, therefore, appears to be the 218th case on record. Reynolds and Morrison[4] state that only one such anomaly has appeared in sixteen years at the Bellevue Hospital. Stukowsky and Boran[8] found only one case in a hospital experience covering 50,000 cases. It has been pointed out recently by Brenneman that the apparent rarity is probably due to failure in diagnosis.

EMBRYOLOGIC CONSIDERATIONS

The trachea and larynx are developed as an outgrowth from the entodermal alimentary canal. The first step in the development of the pulmonary system is a pouching of the ventral wall of the esophagus throughout its entire length. This ventral wall or groove deepens until its edges finally meet and fuse. In this manner the groove becomes a tube which is separated from the esophagus, beginning at the gastric end and extending toward the pharynx. This separation is not complete, however, until a bifurcation takes place—the bifurcation or pulmonary portion below. The tube above does not as yet separate. The

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evagination consists at first only of entoderm, but it fuses later with mesoderm. The epithelial lining of the air passages springs from entoderm, while the basic structure springs from mesoderm. The trachea is the elongated stalk of the pulmonary system. At an early period, two dorsoventral ridges appear at the junction of the trachea with the esophagus. Interference of mesoderm with entoderm at this site would explain the causation of fistula.

REPORT OF CASE

History.—J. G., a girl, aged 5 hours, was admitted to the hospital on July 5, 1926, at 1 a. m. on the morning of its birth. The reason the child was admitted was that its mother, a graduate nurse, aged 24, had a retained placenta. This was her first pregnancy, and, except for the retained placenta, she had a normal delivery. There was no history of malformations or anomalies in the families of either parent. On the morning of admission the child became cyanotic at intervals, but these cyanotic attacks bore no relation to its attempts at feeding. It would not take nourishment, and there was considerable mucus in its throat which had to be aspirated at times. It passed a great deal of meconium. Attempts to feed the baby with a medicine dropper the following day were fruitless, and it was then fed by rectum.

Physical Examination.—The patient, a fairly well developed infant with slight icterus, who weighed 5 pounds and 14 ounces (2,665 Gm.), did not make any effort to cry when awakened or molested. Mucus was coming from its mouth. The temperature was normal. The results of general physical examination at this time were negative, except that a faint murmur was heard over the mitral area. From the history of the case and from the child's actions in the hospital, a congenital esophageal obstruction was suspected, and the infant was taken to the fluoroscopic room where a catheter was passed and a plate study made. The report by Dr. P. B. Mulligan was as follows:

> In view of the clinical suspicion of a possible esophageal obstruction, a small amount of barium milk mixture was given the baby by mouth under fluoroscopic observation. The mixture descended only about as far as the suprasternal notch when it was regurgitated. Next a small catheter was passed through the nose into the esophagus; the catheter could be passed to about the level of the third rib anterior where it met with an obstruction; when force was exerted, the catheter coiled upon itself, forming a loop about 2 cm. in diameter. With the catheter in the esophagus some of the barium milk mixture was allowed to run into the catheter; this mixture collected in a pouchlike enlargement of the esophagus, the lower border of which was on a level with the third rib anterior; this enlargement was about 2.5 cm. wide and 3.5 cm. long; its borders were smooth in outline and extended posterior to the esophagus proper. Observation two hours later showed that none of the barium had entered the stomach; there was no barium in the lungs.
>
> Roentgen-ray Diagnosis: Congenital atresia of the esophagus with congenital diverticulum. This patient, it was noted, had thirteen ribs on each side.

Immediately after this report was made, the child was prepared and taken to the operating room; under local anesthesia, the abdomen was opened through a high left rectus incision, and the stomach was exposed. It was impossible to pass a catheter through for bouginage because of the atresia of the esophagus. After a Weitzel gastrostomy had been performed, the child was returned to its room, and despite all efforts to save it, died that night from the shock of the operation, which was aggravated by its debilitated condition.

Autopsy.—Consent for partial autopsy was granted, and the following facts were noted: The child had a double uterus. The esophagus ended blindly in a

Fig. 1.—A fine catheter inserted through the nose and ending in the esophageal diverticulum. The diverticulum is filled with barium. There are thirteen ribs on either side.

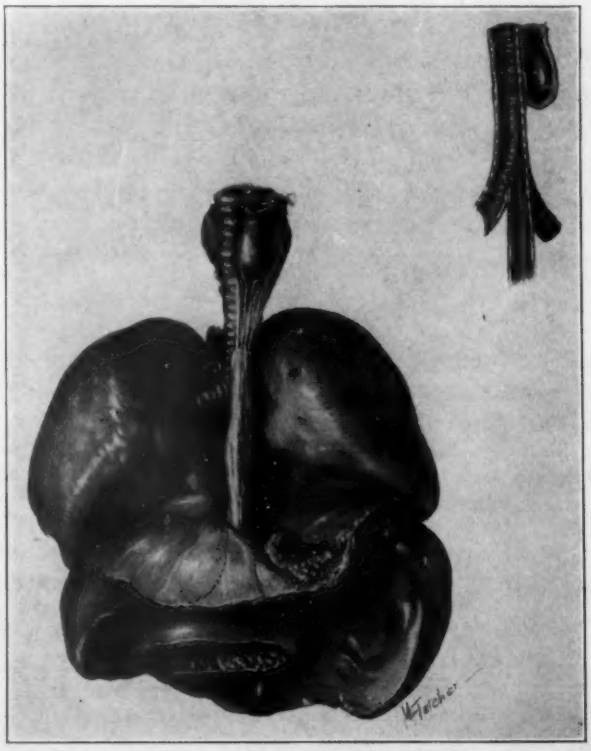

Fig. 2.—Posterior view of gross specimen showing the esophageal diverticulum above. The fibrous filaments replace the absence of esophagus and extending from the blind end of esophagus below to the esophageal diverticulum above. Insert shows a cross-section of the diverticulum and the fistula between trachea and esophagus.

diverticulum about 3 cm. below the pharynx. The lower portion of the esophagus ended blindly above and did not communicate with the diverticulum. A probe was passed from the stomach through the esophagus. It made its appearance in the trachea and emerged in the larynx. The cyanotic spells were explained on the basis of gastric secretion being eructated through the esophagus and by means of the fistula into the trachea.

CONCLUSIONS

1. Congenital tracheo-esophageal fistula is a rare diagnosis and is usually based on postmortem observations.

2. The diverticulum is easily demonstrated by the roentgen ray.

3. Tracheo-esophageal fistula must be considered as a cause for cyanosis in infants.

4. The development of this anomaly is based on embryologic considerations.

CARDIAC OUTPUT IN THE DOG DURING ETHER ANESTHESIA

II. THE EFFECT OF THE INJECTION OF ALKALI ON THE CARDIAC OUTPUT OF THE ANESTHETIZED DOG *

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In a previous communication,[1] it has been shown that the cardiac output of the dog's heart is increased during an ether anesthetic. This change was associated with an increase in the hydrogen ion concentration of the blood. Boothby [2] first suggested that the H-ion concentration regulated the cardiac output of the heart. Douglas and Haldane [3] reached the same conclusion from studies on man. A similar view has been expressed by Means.[4] Harrison, Wilson and Blalock [5] found that the production of respiratory obstruction and the injection of acid were associated with an increase in the H-ion concentration of the blood and an increase in the cardiac output, and that the injection of alkali resulted in the reversal of these two functions. They concluded that the changes in the cardiac output of the heart were dependent on alterations in the H-ion concentration of the blood.

The object of the present study was to determine whether an alkalosis produced by the intravenous injection of alkali was accompanied by an increased cardiac output during ether anesthesia.

METHOD

The method used was described in detail in the former paper.[1] In brief, it was as follows:

Dogs were anesthetized with morphine (0.04 to 0.08 Gm.). It has been shown that this drug has relatively little effect on the cardiac output of normal dogs. About an hour after the administration of morphine, control determinations were performed without ether or alkali. The oxygen consumption was determined by

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*From the Department of Surgery, Vanderbilt University.

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a Benedict spirometer with the graphic recording device. Arterial blood was obtained by puncture of the left ventricle or femoral artery; venous blood, by puncture of the right ventricle. The oxygen and carbon dioxide contents of the arterial and venous blood were determined. The circulatory minute volume was calculated from the Fick formula:

$$\frac{\text{Cc. } O_2 \text{ consumed per minute}}{\text{Amount } O_2 \text{ taken up in lungs by 1 cc. of blood}} = \text{Number of cc. of blood flowing through lungs per minute.}$$

p_H determinations were made by the method of Hastings and Sendroy.[6]

Ether anesthesia was then administered through an open cone, usually until the lid reflexes were abolished. The cardiac output was again determined. The method of Austin[7] was employed for determining the carbon dioxide content in the presence of ether.

In three of the five animals, the anesthetic was discontinued immediately after this determination, and alkali was injected intravenously. In the remaining two animals, alkali was injected while the anesthetic was continued, but to a lighter degree. Further determinations were made at variable intervals on the effects of alkali injection on cardiac output of dogs that were anesthetized previously and also on the output of the heart while the anesthetic was carried to approximately the same degree as that used in the control period. The alkali which was employed was normal sodium carbonate, and the amount varied from 40 to 100 cc.

RESULTS

The animals remained quiet throughout the experiments. The changes which were encountered during the control anesthetic period (without alkali injection) have been described previously.[1] The most striking of these were the increased cardiac output, the decreased coefficient of utilization, the increased hydrogen ion concentration, the decreased carbon dioxide content and, in some instances, the decrease in the percentage saturation of the arterial blood.

The effects of injecting alkali immediately after discontinuing the anesthetic were noted in two animals (tables 4 and 5). The cardiac output was essentially the same as it had been during the anesthetic period. Harrison, Wilson and Blalock[8] have reported marked reduction in the cardiac output of normal dogs following the injection of alkali. It seems likely from the present experiments that the ether effect predominates over that of the alkali, and hence accounts for the failure of the cardiac output to decrease following the injection of alkali. The carbon dioxide content and the p_H were increased markedly by the administration of alkali.

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TABLE 1.—*The Effect on the Cardiac Output of (1) Ether Anesthesia and (2) Alkali and Ether*

Date	Weight, Kg.	Temperature, Fahrenheit	Pulse Rate per Minute	Arterial Oxygen, per Cent by Volume	Venous Oxygen, per Cent by Volume	Arteriovenous Difference, per Cent by Volume	Arterial Carbon Dioxide, per Cent by Volume	Venous Carbon Dioxide, per Cent by Volume	Oxygen Consumption, Cc. per Minute	Cardiac Output, Cc. per Minute	Output per Kg. per Minute, Cc.	Output per Beat, Cc.
6/18/26, 3:30 p. m.: Control study, 1 grain morphine..	10	101.6	50	16.90	12.31	4.58	36.18	38.99	73.8	1,611	161	32
5:00 p. m.: After 20 minutes anesthetic	10	102	120	17.64	15.86	1.78	35.78	36.04	84.9	4,770	477	40
5:50 p. m.: 20 minutes after 40 cc. twice normal sodium carbonate intravenously..	10	102.2	140	17.05	13.49	3.56	52.93	55.74	70.11	1,969	197	14
9 p. m.: 3 hours after giving alkali and ether.....	10	101	60	19.54	12.78	6.76	38.46	43.82	73.8	1,092	109	18

Protocol: 6/18/26: At 2:15 p. m., one grain (0.06 Gm.) of morphine was given. At 3:00 p. m., tracheotomy was performed. At 3:30 p. m., control determinations were made. At 4:40 p. m., ether anesthesia was begun. At 5:00 p. m., eye reflexes were barely obtainable; specimens of blood were drawn. At 5:30 p. m., dog was still anesthetized; it was given 40 cc. of twice normal sodium carbonate. At 5:50 p. m., eye reflexes were barely obtainable; specimens of blood were drawn. At 9:00 p. m., three and a half hours after injection of alkali, and three hours after the ether was discontinued, the dog was walking around and looked well. Determinations were made without an anesthetic.

TABLE 2.—*The Effect on the Cardiac Output of (1) Ether Anesthesia and (2) Alakali and Ether*

Date	Weight, Kg.	Temperature, Fahrenheit	Pulse Rate per Minute	Arterial Oxygen, per Cent by Volume	Venous Oxygen, per Cent by Volume	Arteriovenous Difference, per Cent by Volume	Arterial Carbon Dioxide, per Cent by Volume	Venous Carbon Dioxide, per Cent by Volume	p_H	Oxygen Consumption, Cc. per Minute	Cardiac Output, Cc. per Minute	Output per Kg. per Minute, Cc.	Output per Beat, Cc.
6/19/26, 12:10 p. m.: Control study, ¾ grain morphine	9.7	100	68	22.42	12.64	9.78	36.61	42.17	....	73.8	755	78	11
6/19/26, 1:45 p. m.: Control study	9.7	102	48	22.54	13.12	9.42	37.12	43.12	....	73.8	783	81	16
4.05 p. m.: Anesthesia for 35 minutes	9.7	101	160	23.14	17.65	5.49	23.32	26.71	....	73.8	1,344	139	8.4
5:40 p. m.: After ether and 70 cc. twice normal sodium carbonate	9.7	101	190	20.51	13.24	7.27	42.99	47.19	7.55	73.8	1,015	104	5.3

Protocol: 6/19/26: At 11:30 a. m., three fourths grain (0.04 Gm.) of morphine was given. At 12:10 p. m., control studies were made. At 1:45 p. m., second control studies were made. At 3:30 p. m., anesthetic was begun. The dog stopped breathing once, but eye reflexes were present at 4:00 p. m. when specimens of blood were taken. Animal well relaxed at time. At 4:25 p. m., it was given 20 cc. of twice normal sodium carbonate intravenously. At 5:15 p. m., it was given an additional 50 cc. twice normal sodium carbonate. At 5:20 p. m., ether again was administered. At 5:40 p. m., after ether for twenty minutes, specimens of blood were taken; eye reflexes were easily obtained. The animal was relaxed.

TABLE 3.—*The Effect on the Cardiac Output of (1) Ether Anesthesia and (2) Alkali and Ether*

Date	Weight, Kg.	Temperature, Fahrenheit	Pulse Rate per Minute	Arterial Oxygen, per Cent by Volume	Venous Oxygen, per Cent by Volume	Arteriovenous Difference, per Cent by Volume	Arterial Carbon Dioxide, per Cent by Volume	Venous Carbon Dioxide, per Cent by Volume	p_H	Oxygen Consumption, Cc. per Minute	Cardiac Output, Cc. per Minute	Output per Kg. per Minute, Cc.	Output per Beat, Cc.
6/26/26, 5 p. m.: Control study, ½ grain morphine	11	99	48	16.89	11.65	5.24	41.18	44.15	7.35	70.1	1,338	122	28
6/26/26, 5:50 p. m.: After ether for 15 minutes.....	11	98.6	155	17.25	10.11	7.14	34.43	39.56	7.27	62.7	877	80	5.7
6/27/26, 3 p. m.: After ether for 25 minutes.....	11	98	160	12.72	6.42	6.30	29.75	36.05	7.25	77.5	1,230	112	7.7
6/27/26, 4:35 p. m.: After alkali and during ether...	11	98	200	16.41	8.08	8.33	47.12	52.38	7.50	81.2	975	89	4.9

Protocol: 6/26/26: At 4:00 p. m., one half grain (0.03 Gm.) of morphine was given. At 5:00 p. m., control study was made; no food had been ingested for the previous twenty-four hours. At 5:35 p. m., ether anesthesia was begun. At 5:50 p. m., determinations were made; eye reflexes were abolished completely; the mucous membranes were rather blue.

6/27/26: At 2:40 p. m., ether anesthesia was begun. At 3:00 p. m., determinations were made; the eye reflexes were abolished completely. At 3:30 p. m., under light anesthesia, 40 cc. of twice normal sodium carbonate was injected into the femoral vein. Specimens of blood were taken one hour later; eye reflexes were abolished at the time.

TABLE 4.—*The Effect on the Cardiac Output of (1) Ether Anesthesia and (2) Alkali and Ether*

Date	Weight, Kg.	Temperature, Fahrenheit	Pulse Rate per Minute	Arterial Oxygen, per Cent by Volume	Venous Oxygen, per Cent by Volume	Arteriovenous Difference, per Cent by Volume	Arterial Carbon Dioxide, per Cent by Volume	Venous Carbon Dioxide, per Cent by Volume	p_H	Oxygen Consumption, Cc. per Minute	Cardiac Output, Cc. per Minute	Output per Kg. per Minute, Cc.	Output per Beat, Cc.
6/28/23, 3 p. m.: Control study, 1 grain morphine..	13.3	99.4	50	15.58	10.11	5.47	35.78	40.37	7.42	87.66	1,603	120	32
3:55 p. m.: After 15 minutes anesthesia	13.3	99	120	15.58	12.72	2.86	35.37	37.53	7.37	78.41	2,742	206	23
4:30 p. m.: 15 minutes after 40 cc. of twice normal sodium carbonate	13.3	98.5	100	15.22	11.89	3.33	49.55	53.73	7.53	99.17	2,978	224	30
5.05 p. m.: 35 minutes after alkali and 15 minutes after ether started.....	13.3	97	115	15.22	12.13	3.09	49.08	51.17	7.44	73.8	2,388	180	21

Protocol: 6/28/26: At 2:00 p. m., one grain (0.06 Gm.) of morphine was given. At 3:20 p. m., control samples were drawn; the animal was quiet. At 3:40 p. m., ether anesthetic was begun; determinations were made fifteen minutes later. The eye reflexes were abolished completely. At 4:15 p. m., animal was given 40 cc. of twice normal sodium carbonate into femoral vein. At 4:30 p. m., determinations of cardiac output without ether were made. At 4:50 p. m., ether anesthetic was begun, determinations were made fifteen minutes later; eye reflexes were abolished. It seemed to require less ether to anesthetize the animal after alkali was given, and he was longer in awakening from the anesthetic.

TABLE 5.—*The Effect on the Cardiac Output of (1) Ether Anesthesia and (2) Alkali and Ether*

Date	Weight, Kg.	Temperature, Fahrenheit	Pulse Rate per Minute	Arterial Oxygen, per Cent by Volume	Venous Oxygen, per Cent by Volume	Arteriovenous Difference, per Cent by Volume	Arterial Carbon Dioxide, per Cent by Volume	Venous Carbon Dioxide, per Cent by Volume	p_H	Oxygen Capacity, per Cent by Volume	Oxygen Consumption, Cc. per Minute	Cardiac Output, Cc. per Minute	Output per Kg. per Minute, Cc.	Output per Beat, Cc.
6/29/26, 11:45 a. m.: Control	13	100	32	13.79	7.61	6.18	35.64	42.99	7.47	14.68 94%	103.3	1,672	129	52
1:30 p. m.: After 75 minutes ether	13	98	100	14.87	11.06	3.81	36.45	38.88	7.42	15.39 97%	92.3	2,423	187	24
2:35 p. m.: 45 minutes after alkali..	13	97.5	240	14.27	9.51	4.76	64.53	68.31	7.65	14.30	107.0	2,248	173	9.4
4:10 p. m.: After 50 minutes ether	13	96.6	100	14.57	9.63	4.94	53.19	57.78	7.52	14.62 100%	84.9	1,719	132	17

Protocol: 6/29/26: At 11:00 a. m., one grain (0.06 Gm.) of morphine was given. At 11:45 a. m., the dog was quiet and control study was made. At 12:15 p. m., ether anesthetic was begun. At 1:30 p. m., determinations were made with the dog under ether; the eye reflexes were abolished; the animal was completely relaxed. At 1:50 p. m., it was given 100 cc. twice normal sodium carbonate. At 2:40 p. m., studies to show the effect of alkali were made; no ether was administered at the time. At 3:20 p. m., the administration of ether was begun. At 4:10 p. m., studies were made with the dog anesthetized; the eye reflexes were abolished and the dog was relaxed.

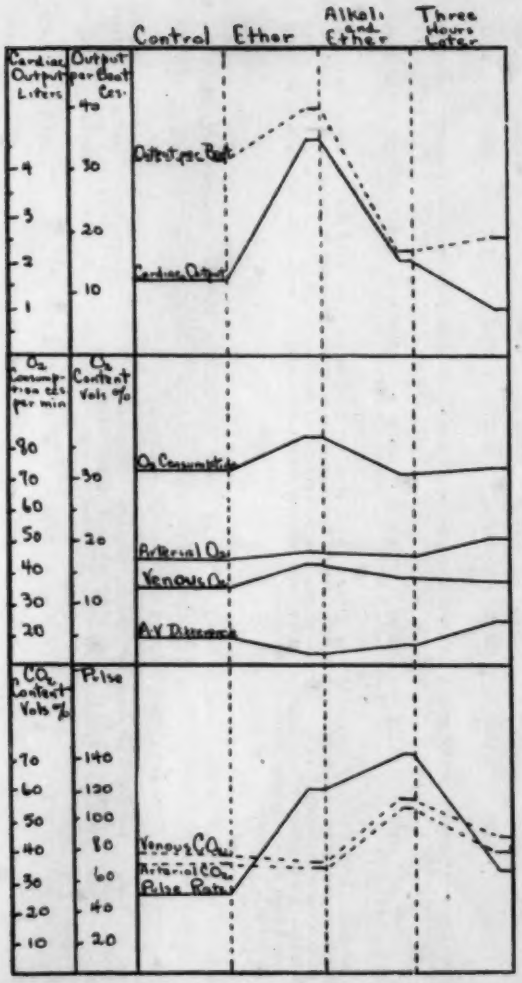

Chart 1.—The values in table 1 are charted in this figure. The increase in cardiac output during ether anesthesia was not so great following the injection of alkali as before, but it did not return to the control line. The decrease three hours later is shown. Alterations in the output per beat in this experiment parallel rather closely changes in the cardiac output. The arterial and oxygen contents approached each other during the anesthetic periods, but less closely after alkali was injected. The carbon dioxide content decreased with ether alone, and increased with alkali and ether.

In this and in the following charts, time relations are neglected.

Determinations made during an ether anesthetic following the injection of alkali as contrasted with those obtained during both the original control period without ether or alkali and the anesthetic period without alkali injection reveal the following changes: The temperature remained

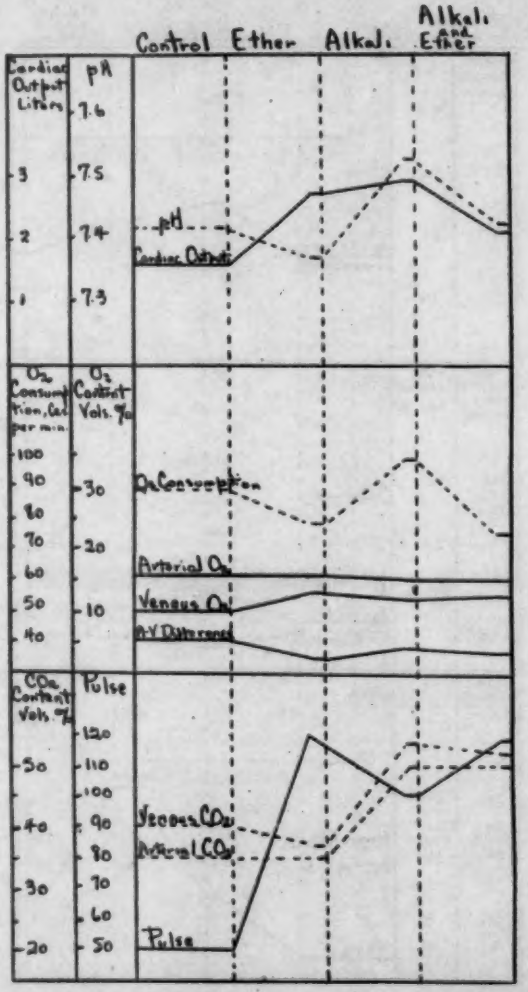

Chart 2.—The points to be noted include the less marked elevation in cardiac output during ether anesthesia following the injection of alkali, the rise in the venous oxygen content while the arterial oxygen content remained stationary and the elevation of the carbon dioxide content. The values in table 4 are charted in this figure.

about the same or fell slightly, and the pulse rate was elevated definitely in four of the five experiments. The oxygen consumption was usually slightly decreased. The oxygen content of the arterial blood remained the same in four instances; in the remaining experiment it was 4 per

cent by volume higher than that obtained in the study of the effect of ether alone, and the same as that during the original control study without ether or alkali. The oxygen content of the venous blood was higher than that found in the control period without ether or alkali and

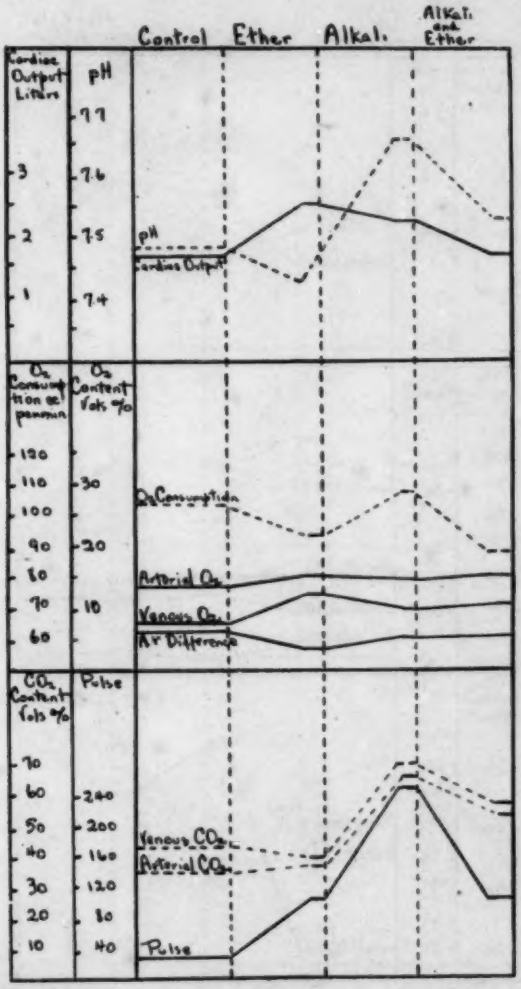

Chart 3. This chart shows that the cardiac output was increased markedly during ether anesthesia before alkali was injected and slightly increased afterward, the oxygen consumption being lower than the control figure in each instance, the increased output was counted for by the decrease in the coefficient of utilization. An acidosis was encountered only in the original anesthetic period. The values in table 5 are charted in this figure.

was lower than that during the original anesthetic period without alkali except for the experiment listed in table 3 in which the animal was deeply anesthetized. The coefficient of utilization was decreased, and the

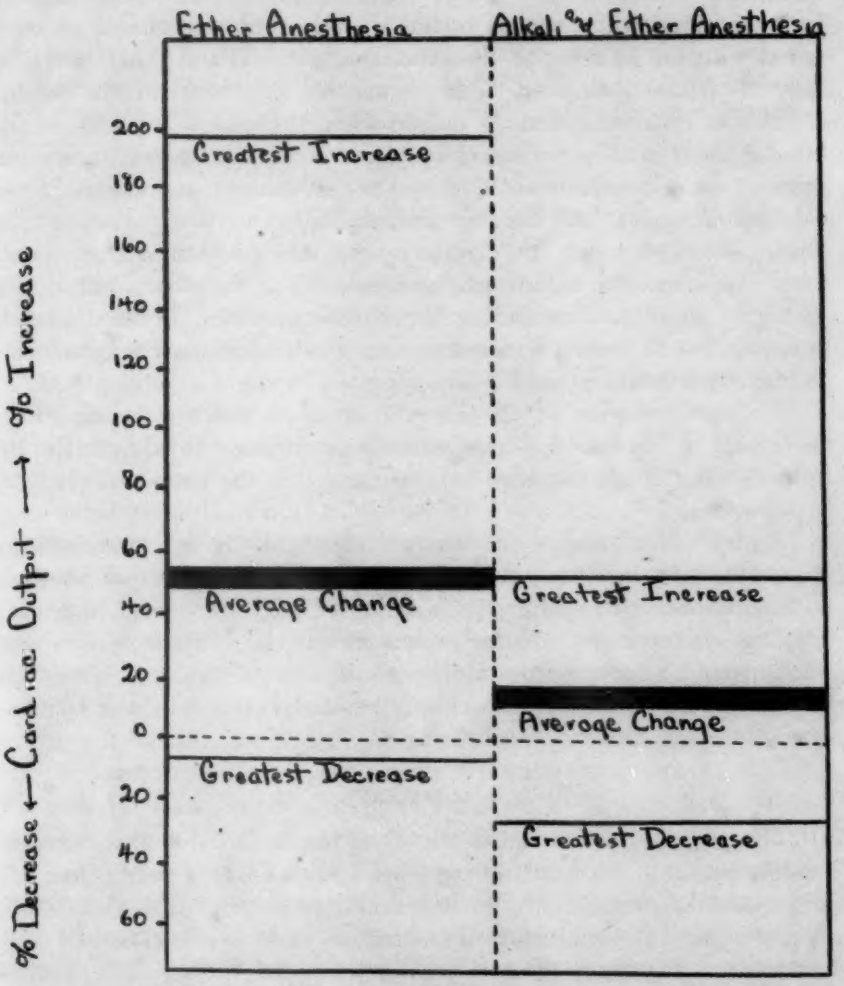

Chart 4.—The percentage change in the cardiac output, under the heading "Ether Anesthesia," was obtained by comparing the figure for the cardiac output during ether anesthesia with that during the control period. The percentage change in the cardiac output under the heading "Alkali and Ether Anesthesia" was obtained by comparing the figure for the cardiac output during ether anesthesia following the injection of alkali with that obtained during the same original control period. The average change is computed from all of the experiments.

It is to be noted that the average increase in cardiac output during ether anesthesia without alkali injection corresponds to the highest figure obtained during ether anesthesia after alkali injection.

cardiac output was increased over that during the control period without ether or alkali, except for the experiment listed in table 3, and in all instances the coefficient of utilization was increased and the cardiac output decreased as compared with the figures obtained during ether anesthesia without alkali (charts 1, 2, 3 and 4). A marked rise in both the arterial and venous carbon dioxide content occurred as compared with the figures for the other two periods, and the H-ion concentration was diminished. The percentage saturation of the arterial blood was not diminished as judged from the oxygen content of the arterial blood in all experiments and from determinations of the oxygen capacity in one experiment (table 5). There was a decrease in the cardiac output per beat in every instance.

In one experiment, the cardiac output was determined three hours after the anesthetic had been discontinued. The cardiac output was distinctly less than that during the previous studies. This drop was probably due to the depressing effect of alkali after the rise occasioned by the ether anesthetic had disappeared.

No measurements of the amount of ether which was used were made, but it seemed that less ether was required to anesthetize the animals after alkali had been injected, and that the period of recovery was prolonged.

It has been noted previously [8] that the H-ion concentration shows little tendency to return to normal after the injection of alkali in a normal animal. After the injection of acid, the return to normal was much more rapid. In the present experiments in which ether was administered after the injection of alkali, the p_H tended to return to normal much more rapidly. This is probably caused by the counteracting effect of the acid metabolites.

COMMENT

The possible causes which might be responsible for the increased cardiac output of the heart during ether anesthesia have been mentioned and discussed previously.[1] Since it has been shown [6] that an acidosis, caused either by partial tracheal obstruction or by the injection of acid, produces an increase in the cardiac output, and that the injection of alkali causes a decrease, it was thought that the rôle of the H-ion concentration in the production of an increased output of the heart during anesthesia could be determined by converting the usual acidosis into an alkalosis by the injection of alkali.

The experiments reported here indicate that a great part but not all of the increase in the cardiac output of the heart may be caused by the increase in the H-ion concentration of the blood. In four experiments the percentage change in the cardiac output during ether anesthesia without alkali was + 196, + 75, + 70 and + 45, while the

corresponding figures during ether anesthesia following the injection of alkali were + 22, + 32, + 49, and + 3, respectively. In the experiment in which the degree of anesthesia was deep, the decrease in the cardiac output during the control anesthetic period was 8 per cent, while during the anesthetic period following the injection of alkali the decrease was 30 per cent.

Henderson [9] and Douglas and Haldane [10] found a decrease in cardiac output with excessive artificial respiration. Grant and Goldman [11] found that this was associated with an alkalosis in which the carbon dioxide tension of the blood was diminished. Alkalosis was produced in the present experiments by the injection of alkali and was associated with an increase in the carbon dioxide content, without any appreciable change in the carbon dioxide tension, and a figure for cardiac output which was less than that for the anesthetic period, but which remained elevated over that during the control period without ether or alkali. Henderson [12] has emphasized the importance of carbon dioxide pressure in the regulation of venous pressure, and hence the diastolic filling and cardiac output of the heart.

Other experiments [13] have demonstrated an increase in the output of the heart during severe anoxemia. The present report (tables 1 to 5) does not suggest this factor as the probable one in causing the increased cardiac output of the heart during ether anesthesia, as evidence of a decrease in the percentage saturation of the arterial blood was not found. The oxygen capacity of the arterial blood was determined in only one experiment, but the arterial oxygen content in all experiments showed practically no variation from that of the control period.

The studies of the effect of ether anesthesia on the cardiac output suggested that the increased output was caused by an increase in the H-ion concentration, by anoxemia, by the direct action of ether itself or by a combination of these factors. It is seen in this report that the output of the heart may remain somewhat elevated in the presence of a p_H which is on the alkaline side and in the absence of a decrease in the percentage saturation of the arterial blood. It is known that ether anesthesia in some instances, causes a decrease in the percentage saturation of arterial blood, but it was not encountered in these experiments. The studies which were made on the effect of ether anesthesia alone were associated with a decrease in the carbon dioxide content of the blood, while in the present experiments the high carbon

9. Henderson, Y.: Am. J. Physiol. **21**:126, 1908.

10. Douglas, C. G., and Haldane, J. S.: J. Physiol. **41**:69, 1922.

11. Grant, S. B., and Goldman, A.: Am. J. Physiol. **52**:209, 1920.

12. Henderson, Y.: Volume Changes of Heart, Physiological Rev. **3**:165 (April) 1923.

13. Harrison, T. R., and Blalock, A. In press.

dioxide content was caused by the alkali injection. Since there was an elevation of the cardiac output in each instance, it does not seem plausible to ascribe this effect to changes in the carbon dioxide content. It seems a likely assumption that the greater part of the increase in cardiac output during ether anesthesia is caused by an increase in the H-ion concentration, as the elevation was much less marked after the injection of alkali. In order to explain the increased output when the H-ion concentration is not increased, it is necessary to assume that there is some direct stimulating action of ether itself. Unless ether has a peculiar action on the peripheral vessels, it is likely that the vasodilation which occurs in acidosis disappears after alkali is injected. Despite the experimental evidence that ether decreases the output of the isolated heart, it is possible that the intact heart may be stimulated directly by ether to pump a greater quantity of blood.

The therapeutic administration of alkalis previous to operations under general anesthesia has been suggested and practiced by many physicians. MacNider [14] recommends the giving of alkalis to prevent the development of anuria, which may occur after a marked reduction in the alkali reserve of the blood. Gwathmey and Tibbetts [15] suggest the giving of sodium bicarbonate previous to a general anesthetic to combat acidosis. Richardson [16] emphasizes the importance of giving alkalis before long operations. However, Meyers and Booher [17] caution against the uncontrolled administration of alkali. They report uncompensated alkalosis following the administration of sodium bicarbonate, following roentgen-ray treatment, after continued vomiting and following prolonged elevations of temperature. Koehler [18] found that the H-ion concentration is decreased during an acute clinical fever. Fever and vomiting are common sequelae of anesthesia, and from this point of view, one should be cautious regarding the indiscriminate administration of alkali. Moreover, evidence that acidosis of short duration per se exerts a harmful effect is lacking. A still more valid objection to the use of alkali lies in the fact that the length and depth of the anesthesia and, consequently, the degree of acidosis, cannot be estimated previous to the operation. Hence, the amount of alkali needed cannot be known

14. MacNider, W. de B.: Anurias Occurring in Normal Animals During Use of General Anesthetics, J. Pharm. & Exper. Therap. **15**:249 (June) 1920.

15. Gwathmey, J. T., and Tibbetts, E. S.: A Preliminary Report on Laboratory Experiments to Determine Value of Certain Agents in Connection with Surgical Operations, M. Rec. **98**:1021 (Dec. 18) 1920.

16. Richardson, F. L.: Heart Lesions in Anesthesia, Am. J. Surg. (anesthesia supplement) **33**:109 (Oct.) 1919.

17. Meyers, V. C., and Booher, L. E.: Some Variations in Acid-Base Balance of Blood in Disease, J. Biol. Chem. **59**:699 (April) 1924.

18. Koehler, A. E.: Acid-Base Equilibrium; Clinical Studies in Alkalosis, Arch. Int. Med. **31**:590 (April) 1923.

unless repeated determinations of the alkali reserve and the H-ion concentration are made during the operation, and this is impracticable. The evidence presented in this paper suggests that alkali may be of value in preventing overstrain of the heart, but it is possible that such treatment may have other untoward effects.

SUMMARY

The cardiac output of the heart of the morphinized dog has been determined during ether anesthesia both with and without the injection of alkali. The changes in pulse rate, temperature readings, oxygen consumption, arterial oxygen, venous oxygen, arterial carbon dioxide, venous carbon dioxide, H-ion concentration and cardiac output have been observed. The following statements are believed to be true for the dog:

1. The percentage increase in the cardiac output of the anesthetized dog is reduced by the injection of alkali.

2. The increase in cardiac output persists during ether anesthesia in the presence of an alkaline p_H, but to a lesser degree than when acidosis is present.

3. The increase in cardiac output is not dependent on anoxemia.

4. The carbon dioxide content is elevated during ether anesthesia following the injection of alkali, whereas it is lower than normal during ether anesthesia without alkali injection.

5. The alteration in the cardiac output of the heart cannot be attributed entirely to the effect of changes in the hydrogen ion concentration of the blood, and that there is some direct stimulating action by ether must be assumed.

The objections to the use of alkali have been discussed. Without further information, the routine administration of alkali before operations does not seem advisable.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 792)

URETER

Ureteral Transplantation.—Smitten[25] compiled 318 cases of implantation of the ureters into the intestine, not including the Maydl type of operation. Two hunded and twenty-two were in women, and forty-nine in men. The statistics of the operations were as follows: fistula of the bladder, 156 cases, with death in thirty-four (21.8 per cent); anomalous conditions, fifty-eight cases, with death in eighteen (31 per cent); malignant tumors, ninety-eight cases, with death in sixty-one (63 per cent); inflammatory processes, four cases, with death in three (75 per cent). Of the total number of patients, 116 died and 200 recovered; in two cases the result was not known. Thirty patients died from peritonitis, twenty-one from urinary infection, five from pneumonia and three from tuberculosis. The late results from six months to ten years were known in seventy-one cases. In six of these death was caused by renal insufficiency; in three by recurrence of the original condition, and in two, by intercurrent disease. After the first operations, there usually was considerable inflammatory reaction in the rectum that at times either caused perforative peritonitis or ascending infection in the kidney. Suture infection was observed in ten cases.

Bégouin,[26] reviewing his cases of ureterocystoneostomy, states that in cases of accidental or voluntary section of the ureter this operation, which is simple and only requires a few minutes, adds little to the

25. Smitten, A. T.: Ueber die Einpflanzung der Ureteren in den Darm, Ztschr. f. urol. Chir. **19**:219-220, 1926.

26. Bégouin, P.: De l'insuffisance fonctionnelle du rein apres l'ureterocystoneostomie, Arch. franco-belges de chir. **29**:81-85 (Feb.) 1926.

gravity of the operation. Of six of Bégouin's patients, seen from six months to three years after operation, none presented normal ureteral permeability or good renal function. In two cases there was complete obliteration of the implanted ureter; in one, stricture at its end had caused hydronephrosis, and in another there was a large orifice, permitting marked ureteral reflux. In a fifth case pyelonephritis necessitated nephrectomy. The last case, although the orifice was apparently normal and the ureter permeable, showed marked diminution of the urea output on the side of operation. In most cases ureterocystoneostomy, like circular suture and all the different types of reimplantation or anastomosis of the ureter, brings about, in a variable period of time (rarely exceeding two or three years), functional destruction of the kidney. If the destruction occurs gradually the condition is not serious, but in most cases there is a rapid onset of an intermittent hydronephrosis or renal infection, sometimes leading to urgent nephrectomy. Bégouin concludes, in accord with a number of leading surgeons, that this operation should be abandoned and if necessary replaced by the old ureteral ligation followed by nephectomy. He suggests making this ligation high up above the operative field, after the presence of the other kidney has been determined by palpation and the peristaltic waves of the intact ureter have been seen. Nephectomy is not necessary in all cases. If it is indicated, it may safely be performed from eight to fifteen days after the preceding operation.

[Ed. Note.—This is a definite and interesting review of a series of cases which partially settles a much debated question, the disposition of the destroyed or severed ureter. While the number of cases cited is small, they show in a fairly conclusive way that if the opposite kidney is intact, conservative surgical measures are not usually indicated.]

Ureteral Ligation.—Helmholz and Field [27] report the results of an extensive experimental study of the effects of ligation of the ureter in rabbits. They have paid special attention to early and acute changes. Opinions from the literature are quoted. The changes that they find in the pelvis are: (1) hemorrhage, edema and exudation of leukocytes, which begin after four hours and reach a maximum in from eighteen to twenty-four hours; (2) destruction of small or large areas of the epithelial lining of the pelvis leading to ulcers or deep sterile abscesses in the peripelvic tissues; (3) healing beginning after forty-eight hours by the proliferation of connective tissue cells and the removal of the destroyed leukocytes by polyblasts; (4) healing of the small lesions of the pelvis by the formation of a pyogenic membrane and the lateral

27. Helmholz, H. F., and Field, R. S.: Acute Changes in the Rabbit's Kidney, Particularly the Pelvis, Produced by Ligating the Ureter, J. Urol. **15**:409-429 (May) 1926.

ingrowth of pelvic epithelium; (5) the formation of small diverticula by the action of the irritant urine when large openings have allowed the urine to reach far into the tissue, and (6) the replacement of the normal fat and connective tissue about the pelvis by dense fibrous connective tissue.

The changes in the kidney proper consist of: (1) exceptionally, focal necrosis of the epithelium with leukocytic infiltration; (2) exceptionally (only once in this series), infarction of the kidney, and (3) necrosis of the tubules of the papilla, exceptionally, with necrosis of the entire papilla.

The relation of these experiments to the pathology of pyelitis in man can be summarized as follows: (1) certain hemorrhages (evidence of which is found after death) in the pelvis of the kidney following obstruction of the ureters may be attributed to pressure and not necessarily to infection; (2) the formation of diverticula of the pelvis might give rise to sterile pyuria that persists for a long time; (3) the products of acute inflammation can be removed so rapidly as to leave practically no trace after a period of fourteen days, and (4) the necessity of controlling results in experiments on the injection of bacteria into the pelvis, when the ureter is obstructed, is evident since the presence or absence of infection makes no marked difference in the gross and microscopic appearance of hydronephrotic kidneys during the first twenty-four hours.

Calculi.—Hourtoule [28] reports the case of a married woman, aged 22, who had suffered attacks of colic from ureteral stone for seven years. A small hard mass, 2 cm. in diameter, was felt in the left culdesac; roentgenologic examination proved this to be a stone. The left kidney, which was found to be almost functionless at cystoscopy, also contained stones. The patient became pregnant and gave birth normally to a healthy child. After pregnancy the attacks of colic returned, and this time were accompanied by fever. At operation a voluminous left hydronephrotic kidney was removed. The ureteral stone was left in place. Two years later, she was perfectly well; the ureteral stone had not caused any trouble.

Bumpus and Scholl [29] report a series of 880 cases of ureteral stone treated at the Mayo Clinic. Of these, 640 were removed surgically and 240 were removed by cystoscopic manipulation during the later years. Six hundred and forty-eight operations were performed in 640 cases, eight of which were bilateral. The following types of operation were performed: ureterolithotomy, extraperitoneal, 522; pelviolithotomy,

28. Hourtoule, V.: A propos d'un calcul de l'uretère, J. d'urol. méd. et chir. **20**:318-319, 1925.

29. Bumpus, H. C., Jr., and Scholl, A. J.: Ureteral Stones, Surg. Clin. N. Amer. **5**:813-827 (June) 1925.

twelve; nephrectomy, thirty-three; nephro-ureterectomy, forty-eight; resection of one half of horseshoe kidney, one; exploration, stone not found (found in bladder later in five cases), thirteen; pelviolithotomy and ureterolithotomy, six; nephrolithotomy and ureterolithotomy, two; ureterectomy, partial (kidney removed previously), three; transperitoneal ureterolithotomy, one; removal through vagina, one, and transvesical ureterolithotomy, six.

The incision for ureterolithotomy varies with the site of the stone. If it is the upper third of the ureter, or if there is also an associated stone in the renal pelvis, a posterolateral incision is made. It is not necessary to extend the incision as far posteriorly as is usual in operations on the kidney. The upper third of the ureter and the ureterovesical angle may be exposed readily without delivering the kidney. In some cases the stone may be brought up into the pelvis and removed through a pelvic incision; this is especially desirable if stone is also present in the kidney.

If the stone is in the iliac or the pelvic portion of the ureter, a straight rectus incision gives the best exposure. The exact location of the incision depends on the site of the stone. If the stone is in the lower segment, the incision through the rectus muscle should be made directly down to the pubic bone and should be of ample length. The peritoneum is pushed toward the median line until the iliac vessels are uncovered. If not fixed by inflammatory or postoperative adhesions to the surrounding tissues, the ureter generally follows the retracted peritoneum and is found on its posterior surface. In cases in which the ureter is dilated, it may be readily located. In other cases, the palpation of the stone may determine the position of the ureter.

The position of the majority of stones in the lower portion of the ureter makes their manipulative removal possible in many cases. The two essentials to success in the cystoscopic removal of stones are adequate dilatation of the ureter and the shifting of the axis of the stone.

The first can be accomplished by the use of a dilator or by passing increasingly larger catheters or sounds up the ureter past the stone or by passing up several catheters at the same time. The authors prefer the latter method, since the stone on several occasions has lodged between the multiple catheters and been removed with their withdawal. Usually such catheters are left in place for forty-eight hours; then each one is twisted separately and all are withdrawn together. Some stones will pass with the next voiding; most will be recovered within the first two days, and a few will pass after a week. When the stone becomes impacted in the wall of the bladder, its removal will be hastened by slitting the ureterovesical orifice.

Eighteen of the 240 stones removed by manipulative methods were in the middle third of the ureter, 118 in the lower third, sixty-three at the ureterovesical juncture, and twenty-four were intramural. Sixty-

four of the 648 stones removed by surgical methods were at the ureteropelvic juncture, seventy-one in the lumbar segment, forty-one in the middle or iliac segment, eleven at the iliac crest, 311 in the lower third, eighty-eight at the ureterovesical juncture, and thirty-six were intramural.

The kidney was removed in eighty-one cases. In forty-eight cases the ureter also was removed, in most instances completely. In most of these the kidney had been partially or completely destroyed as a result of ureteral obstruction. In a few cases there were also stones in the kidney. In most of the cases in which nephrectomy or nephroureterectomy was performed, the kidney was exposed through a posterolateral incision. If the stone could then be reached, the kidney and segment of ureter were removed. If the stone was in the middle or lower third and the ureter dilated and the stone impacted, the vascular pedicle was cut and ligated, and the kidney left hanging from the anterior angle of the wound. The patient was then turned over and an anterior rectus incision made, through which the ureter was isolated and cut below the stone. The ureter was freed as far as the point reached from the posterior incision and then drawn through the posterior wound while still attached to the kidney. It is usually desirable to leave a long strand of catgut or silk fastened to the retreating ureter so that the lower end of the ureter may be recovered if it does not readily pass through into the area of the posterior incision.

Tumor.—Stewart,[30] reviewing the literature from 1922 (when Aschner had compiled forty-seven cases of primary tumor of the ureter) found five other cases recorded and reports an additional case. These rare tumors occur most frequently during the sixth decade of life.

Calculus is not a common predisposing factor; when present it is generally associated with malignant forms of tumor. Pathologically, these tumors usually are papillary in type and many show the structure of benign papilloma, in which case they may be multiple or diffuse. There is a decided tendency toward malignancy: papillary carcinoma, medullary carcinoma and squamous epithelioma occur. Sarcoma is rare. Any portion of the ureter may be involved, although there is evidently a predilection toward either the upper or the lower extremity.

The symptoms produced are not pathognomonic of the disease, and are the same as those engendered by renal neoplasms, namely, hematuria, pain and sometimes renal enlargement due to the tumor obstructing the ureter and causing hydronephrosis. Accurate diagnosis usually is difficult, but considerable aid is obtained from the employment of ureteral catheterization and pyelo-ureterography. It is important to locate the

30. Stewart, R. L.: Primary Tumors of the Ureter, Brit. J. Surg. **13**:667-682 (April) 1926.

downward extent of the tumor, with special reference to the possibility of multiple growths.

Radical operation is indicated in treatment. In most instances nephro-ureterectomy, either complete or partial, is the method of choice. Fulguration of tumors situated at the lower end of the ureter has given encouraging results in cases unsuited for the more radical surgical measures.

BLADDER

Diverticula.—Lurz [31] differentiates true diverticulum of the bladder and trabeculation. The true diverticulum contains muscle fibers and connective tissue representing the vesical wall as well as the lining of epithelium. False diverticula, such as those produced by rupture of abscesses into the wall or pericystic phlegmons, are considered as a separate group.

The microscopic picture of the true diverticulum shows that it never corresponds entirely to the normal vesical wall. The epithelial layer is thinner, lacking in the usual layering, and the wall consists for the most part of connective tissue with lymphocytic infiltration and a few muscle fibers. In form diverticula may be cone-shaped, oval, pear-shaped, angular (if attached to contiguous organs), round, or saccular. In number they may vary from one to forty.

Lurz has compiled from the literature 1,407 cases of so-called congenital diverticulum. To these he adds nine cases from Enderlen's clinic at Heidelberg. Only thirty-nine cases occurred in women. Three were found in fetuses. The majority occurred in men more than 50 years of age.

From the standpoint of etiology Lurz believes that true congenital diverticula do not occur. The various theories based on anatomic and embryologic studies to show that diverticula develop from anomalies in the embryo are reviewed. Kaufmann believes that the region of the lateral wall of the bladder in front of the ureteral orifices, the base of the bladder beyond the interureteric ligament, and the vertex of the bladder corresponding to the vesical end of the urachus are predisposing points for the development of diverticula. Thus, anomalous developments of the rests of ureteral buds, of the urachal ending in the bladder, and the like, might give rise to diverticula. It has not been demonstrated that intra-uterine obstruction of the urinary tract is a causative factor. If this were true there would be, according to Lurz, concomitant hydro-ureter and hydronephrosis. He states that there is probably some developmental weakness in certain portions of the vesical wall but that the diverticulum itself develops as a pulsion sack. The

31. Lurz, L.: Ueber sogenannte kongenitale Blasendivertikel, Ztschr. f. urol. Chir. **18**:278-299, 1925.

development of diverticula is most common in association with such obstructions of the urinary tract as prostatitis and prostatic hypertrophy afford. With the enlargement of the diverticulum the bladder itself becomes filled with each relaxation of its neck. Thus, marked detrusor hypertrophy develops. The contraction of the bladder is partly used in further distending the diverticulum so that a condition exists somewhat analogous to valvular insufficiency in the heart. Lurz has shown by experiments, with one catheter in the diverticulum and another in the bladder, that the pressure according to manometric readings is less in the diverticulum than in the bladder itself.

Symptomatically, the relative youth of the patient, lack of frequency at night, longer duration of symptoms, change in the degree of difficulty of urination from time to time, slowness of the emptying of the bladder with absence of stricture, prostatic hypertrophy or disease of the spinal cord, the occurrence of stone shadows in the roentgenogram of the bladder, when these stones are not demonstrated by cystoscopy, residual urine and infection serve to differentiate the condition from prostatic disease. In some cases in which the diverticulum is attached to the rectum, defecation is painful or the bladder can be emptied only on sitting as at defecation. Hematuria may occur at times or there may be ureteral colic from compression of the ureteral ostia.

The diagnosis is based on urologic study such as cystoscopy, and roentgen-ray studies of the bladder, filled with an opaque medium (cystography), or after an opaque catheter has been inserted into the diverticular orifice. Lurz reviews the technic and precautions necessary with these procedures.

The treatment of the condition usually advised is radical surgical excision. A few urologists advocate drainage of the diverticulum by indwelling catheters and lavage of the sac with silver preparations, but these are in the minority. The utmost care is urged in the study of the urinary function before surgical treatment is undertaken. Differential tests of function, study of retention of blood urea, and the investigation of the urinary tract for infection, must be gone over carefully. Any gross infection should be treated and ameliorated, if possible. The various operative procedures are outlined. Lurz prefers the suprapubic transverse incision after elevation of the pelvis. The disadvantages of Voelcker's parasacral route are brought out. The extraperitoneal, extravesical operation in most cases is ideal. The next best procedure is the extirpation of the diverticulum from within the bladder. The dangers to rectum or ureters from operative procedures, and the precautionary measures to protect these structures (such as placing catheters in ureters before operation or injecting indigocarmin), are emphasized. At times it is necessary to transplant the ureters. Geraghty's resection of the mucosa from the diverticular neck with closure and extravesical drainage of the diverticular sac is cited.

Division of the diverticular neck intravesically is practiced by some when the diverticulum is situated close to the internal sphincter or goes deeply toward the rectum.

Lurz emphasizes the importance of abating prostatic hypertrophy or other urinary obstruction either at the same operation or before or after the excision of the diverticulum. Different authors recommend a different order of operative procedures under these circumstances, but to remove the obstruction and not the diverticulum, or vice versa, leaves the result unsatisfactory.

[ED. NOTE.—This is an excellent review, and the opinions of most of the leading urologists on the subject are brought together. Certainly conservative treatment can lead only to a poor result, while the operative mortality is not excessive and the end-results of surgical treatment are on the whole good. Many points in the treatment of vesical diverticula are open to argument, especially as to technic of approach, type of excision, the treatment of tumors and prostatic hypertrophy at the same or a subsequent time. More studies of the type that Lurz has presented will aid in the solution of these problems and may help to lower the operative mortality, in the same manner as that of the enlarged prostate has been lowered.]

Nerve Control.—Grouvall [32] reports his experimental work on the nerve control and mechanism of micturition. His experimental procedures were divided into the following stages: (1) The bladder was filled with urine; (2) the intravesical pressure was raised until equal to that of a column of water 12 cm. high; (3) rhythmic contractions of the bladder were then observed; (4) an afferent impulse was then given to the bladder through the nerves erigentes and hypogastrici, which caused a contraction of the detrusor muscle and an increase in the intravesical pressure up to 30 cc. of water; (5) the sphincter vesicae was dilated reflexly and the urine passed into the urethra; (6) the bladder emptied itself, and (7) the last few drops of urine were expelled through rhythmic contractions of the smooth and striated muscles surrounding the urethra.

PROSTATE

Electrocoagulation.—Walker,[33] realizing the value of punch operations in selected cases of prostatic obstruction, and preferring diathermy to galvanocautery, as used in Caulk's instrument, devised a new instrument. In external form it resembles the Young punch, but the sheath is constructed of bakelite, an excellent insulating material allied to

32. Grouvall, H.: Mechanismus der Blasenentleerung, Ztschr. f. urol. Chir. **19**:173-174, 1926.

33. Walker, K. M.: A New Diathermy Punch for Prostatic Obstruction, Proc. Roy. Soc. Med. (Sect. Urol.) **18**:35-38 (Aug.) 1925.

vulcanite, with a metallic lining. This lining only comes to the surface at the edge of the window situated below the beak; elsewhere it is insulated from the urethra by the bakelite covering.

The punch is introduced with an obturator in position, and, to facilitate its insertion in difficult cases, a pliable bougie guide may be attached to the beak by means of a screw. When it is in position the obturator is withdrawn, and a system consisting of a telescope, a lamp and inlet and outlet tubes for irrigation is substituted, thus converting the instrument into a posterior urethroscope of the Gueringe type. Under guidance of the eye, the punch is now withdrawn until the bar is seen to engage the window. Once it is in position, the instrument is held firmly and pressure is exerted on the bar by slightly raising the proximal end. Connection is then made with the source of diathermy current. When the current is turned on, the inner metallic layer of the sheath immediately becomes a urethral electrode but, owing to the insulation conferred by the bakelite covering, the only point of contact with the urethra is the edge of the window engaging the bar. From this edge a line of coagulation can be observed to spread within ten or fifteen seconds; this whitens the whole area of prostate engaged. By maintaining continuous irrigation, the process of diathermy can be carried out under complete ocular control, the current being turned off when it is judged that a sufficient depth of tissue has been destroyed.

In order to remove the wedge of destroyed tissue, and thus obtain immediate benefit without waiting for the separation of sloughs, the telescope and lighting system is withdrawn and an inner tube, resembling that used in the Young punch, is inserted. By pushing this home and giving it at the same time a slight rotary movement, a core of destroyed tissue, about 2 cm. in length and 0.5 cm. in diameter, may be removed. This does not, however, constitute the whole amount of prostatic tissue destroyed by the operation, the full benefit of which will be obtained later when the sloughs have separated. The telescope and lighting system may then be reintroduced, the area of operation inspected, and a decision made as to whether or not any further fulguration is required. If the operator is satisfied with the amount of tissue dealt with, the bladder is emptied, the obturator inserted and the instrument withdrawn.

The diathermy punch has definite advantages over any similar instrument yet evolved. The operation is not a blind proceeding like Bottini's, but is done under full ocular control. It has an advantage over Young's operation in that it eliminates the risk of hemorrhage, and it allows the easy removal of greater quantities of prostatic tissue, the subsequent sloughing of the diathermy area widening still further the channel dug by the punch.

The type of case in which the diathermy punch can be employed most conveniently is that in which there is a "bar" obstructing the vesical outlet. It may also be used in cases of moderate enlargement in

which prostatectomy is contraindicated, and occasionally in cases of postoperative obstruction and malignant disease.

Hammond [34] reviews briefly the various operative and nonoperative procedures used for the relief of prostatic obstruction. He finds that in selected cases the most gratifying results are obtained by the application of surgical diathermy through an operating cysto-urethroscope. The adenomatous enlargements should be carefully separated from the fibrous ones. With the fibrous and atrophied prostates the urethra is not compressed throughout its length, and the obstruction is at the neck of the bladder. When the bladder is opened in these cases, it will be found that there is a narrowing of the internal meatus, but that, when the finger is passed through this, the prostatic urethra appears more dilated than usual. This type of prostate does not tend to become progressively larger, and the obstruction is localized in the vesical neck; the latter can be easily destroyed and removed, and does not tend to recur. After treatment by diathermy, shock and hemorrhage are never severe enough to cause any worry; the convalescence is much shorter than after prostatectomy, the functional result is better, and the mortality rate is lower. When it is remembered that the type of prostate which is treated by diathermy is that which is largely responsible for the mortality after prostatectomy, it is obvious that a careful selection of cases will lead to an improvement in the statistics of this operation. If there is renal failure or marked infection, Hammond institutes preliminary suprapubic drainage.

Prostatectomy.—Hunt [35] advocates the use of Pilcher's modification of the Hagner bag as being superior to other methods of control of bleeding following suprapubic prostatectomy. Hemostasis in prostatic surgery has not formerly been given the consideration that it has been given in other fields of surgery. It is to be expected that there will be some hemorrhage, which often becomes a serious factor. The various methods of packing the prostatic capsule with tampons, pressure sticks, kephalin gauze and the like are reviewed. Following the removal of such packs granulations are often broken and severe secondary hemorrhage is induced.

Hunt describes his technic of one-stage suprapubic prostatectomy under vision. He supports himself with statistical evidence in the statement that 75 per cent of cases can be safely brought to this one-stage procedure with proper preliminary preparation. He emphasizes the fact that the Mayo Clinic figures formerly showed that the mortality rate was

34. Hammond, T. E.: Diathermy in the Treatment of Prostatic Obstruction, Brit. M. J. **1**:94-95 (Jan. 16) 1926.

35. Hunt, V. C.: Hemostasis in Suprapubic Prostatectomy, Ann. Surg. **83**:381-391 (March) 1926.

higher when the risk was supposed to be moderate, and the usual catheter drainage and other preliminary medication was not given, than when the risk was presumed to be grave and a stringent preoperative regimen was consequently instituted. At the present time all patients are given preliminary treatment, as mentioned, the majority of them being put on catheter drainage.

After enucleation of the prostate under vision, the capsule is sutured, a sound is passed through the penis into the open bladder, and the tube of the Pilcher bag is then drawn out with it through the urethra. The bag is distended with water so that it impinges on the vesical neck. The pressure required is from 60 mm. of mercury (about 60 cc. of water) to 140 mm. of mercury (about 180 cc. of water). A silken cord threaded through the tube of the bag and attached to the base rather than the apex of the bag, is attached to a Hamer tripod under moderate tension, just enough to hold the bag in place and control hemostasis without unnecessarily stretching the prostatic capsule. By this means, the pressure is brought from the base of the bag toward the prostatic bed rather than pulled into the prostatic bed by elastic traction on the urethral tube.

Suprapubic drainage is maintained by placing a 30 F. catheter in the bladder, which is closely sutured around this catheter and around the vesical portion of the tube of the Pilcher bag which extends through the bladder and abdominal wall. Through this suprapubic tube of the bag the water is released in about sixteen hours. If any bleeding occurs, the bag is refilled for a further period. If no bleeding occurs, the bag and vesical catheter are all removed suprapubically eight hours later. As the bag is removed a 16 F catheter, attached to the urethral portion of the tube, is drawn in as an indwelling catheter. Immediate urethral drainage is thus established and prolonged, and messy suprapubic drainage is avoided.

[ED. NOTE.—No one who has seen Hunt work can fail to be impressed by the effectiveness of the method described in his hands. It seems ideal, as does the whole one-stage procedure, and almost perfect from the surgical standpoint. During the last few years the results of suprapubic prostatectomy have equalled in almost every way the low mortality rates of the perineal operation. Certainly, the method described by Hunt fulfils all the requirements of surgical simplicity and efficiency and will be welcomed by those general surgeons and urologists who have not had satisfactory results in the control of hemorrhage from the prostatic bed after operation. The use of a hydrostatic-pressure bag does not appeal to all surgeons as entirely a surgical procedure. Complete hemostasis at the time of operation, together with gauze packing, works effectively in preventing bleeding either directly or some time after operation.

Any procedure that is systematized and carefully worked out and controlled gives better results than varying methods occasionally employed.]

Dodson [36] calls attention to the fact that hemorrhage and shock are second and third in importance as causes of death following prostatectomy. The blood vessels of many old men suffering from prostatic hypertrophy are so sclerotic that they do not compensate well for the loss of fluid from the vascular system. The relief following intravenous injections of sodium chloride solution and of glucose, while important, often is only transitory. Dodson recommends that transfusions of whole blood be carried out more frequently, since they supply the elements necessary to combat the loss of blood cells. Whole blood replaces the lost fluid, improves the quality of the blood and, by decreasing the coagulation time, is a valuable asset in the control of bleeding. Transfusions of whole blood are preferred to citrate transfusions because of the relative infrequency of reactions from the former technic.

Seven cases of prostatectomy in which blood transfusions were employed are reviewed. Four of these were cases of carcinomatous prostate, and in all there was some degree of arteriosclerosis. In two cases transfusion was given because of hemorrhage, in two because of shock, and in three because of gradual failure of the circulation and inability to "rebound." Two of the patients in the last group died. In both there was extensive carcinoma of the prostate, and the risk was extremely grave.

While it is not asserted that transfusion is a panacea, it is held that it is a procedure of merit which should be more frequently employed postoperatively in this class of case, and that as a part of the preliminary procedure the blood should always be matched for blood transfusion.

[Ed. Note.—We believe that the advocacy of transfusion for the patient who is not doing well after prostatectomy is founded on good therapeutic principles. Especially is this true in cases of hemorrhage and shock. The administration of large quantities of sodium chloride solution is by no means to be dispensed with. Transfusion is added as a further supportive measure, and it would seem should often turn the tide toward a satisfactory convalescence.]

Bidgood [37] describes in detail an attachment which can be placed on any ordinary operating table in such a manner that the perineum of the patient can be elevated to the proper level for surgical approach to the prostate or seminal vesicles. The ideal position of the patient for this work is such that the perineum is parallel to the floor. The apparatus is made of steel and aluminum, and its various parts are

36. Dodson, A. I.: The Value of Blood Transfusion in Surgery of the Prostate, Ann. Surg. **82**:974-977 (Dec.) 1925.

37. Bidgood, C. Y.: A Perineal Elevator, Ann. Surg. **83**:126-130 (Jan.) 1926.

simple in operation. While not intended to supplant the use of urologic tables for operative and cystoscopic work such as those devised by Young and others, this apparatus will suffice for those who are not so fortunate as to have access to one of these more elaborate tables.

From the illustrations and sketches appended, the apparatus seems to be simple and adequate, and should fill a need in the equipment of small hospitals.

Dax [38] has observed three cases of obstruction with stricture of the urethra in 150 cases of prostatectomy. In the first case, the obstruction was complete and situated at the deep orifice of the canal at the level of its union with the prostatic pouch; this occurred a week after operation. Dax had taken care not to pull on the adenoma for fear of tearing a portion of the urethral mucosa. He believes that this urethral obstruction was due to the formation of an irregular and exuberant scar. Obstruction in the second case occurred nine months after prostatectomy at the orifice of the bladder, and was due either to a missed piece of adenoma in the prostatic pouch or to the persistence of a diaphragm composed of the prostatovesical mucosa. The first possibility may usually be avoided by careful digital examination of the prostatic pouch after operation; the other results from faulty technic. Obstruction in the third case occurred two months after operation, the result of stricture 3 mm. from the meatus from ulceration caused by the permanent catheter which had been badly tolerated and had caused continuous suppuration. To avoid the last complication, Dax advises the use of sounds of small caliber (15, 16 or 17), and if after antiseptic irrigations the catheter is not tolerated, it is better to remove it and let the hypogastric wound close by itself. The treatment should consist in dilatation, the obstacle eventually being destroyed with the dilator, and catheterization. Rarely, the bladder may have to be reopened.

Andre [39] says that stricture of the urethra following prostatectomy is not infrequent, but that "decentrement" or misalinement of the urethrovesical juncture is rare. In 300 cases in which he performed prostatectomy, ten cases of stricture and two of "decentrement" were found. The cause of strictures is not always known; in five of Andre's cases there had been no difficulty in enucleating the prostate. The stricture occurred from eleven days to nine months after operation. In four cases of stricture, the plane of cleavage had not been clear, and probably a lesion of the mucosa of the membranous urethra resulted. In another case, in which total prostatectomy was necessary on account of the

38. Dax, L.: Obstructions et retrecissements de l'urethre apres la prostatectomie transvesicale, Arch. franco-belges de chir. **29**:101-105 (Feb.) 1926.

39. Andre, M.: Retrecissements et decentrements de l'uretre apres la prostatectomie, J. d'urol. méd. et chir. **21**:374-377, 1926.

impossibility of enucleating the organ, a tight stricture developed. In most of Andre's cases, the stricture was cured by dilatations; in two of them internal urethrotomy was required. In the two cases of "decentrement" the fact that micturition had been easy, without effort and of normal frequency, whereas catheterization had been impossible, led to the diagnosis. These complications can be avoided if care is taken not to tear the urethral mucosa in removing the adenoma. The vesical mucosa should be severed at the bases of the prostatic lobes and not at the top. When a well developed median lobe is present, the mucosa should be removed completely from before backward, so as not to leave floating fragments which might later act as a valve during micturition. In some cases it is advisable to dilate the urethra at monthly intervals following operation.

Rubritius and Schwarz [40] state that contracture of the vesical neck is not an entity, and that the most varied anatomic changes of the sphincter and the nerve supply lead to retention. If the whole group is brought under one name, that name will convey only the meaning of a symptom, namely, retention. The common functional factor in practically all cases of retention is hypertonus of the sphincter, which is the same whether brought about by a small adenoma or by inflammatory contractions. In one group of cases the hypertonia stands out so markedly that it must be considered as the entire cause of the retention. The outstanding method of treatment consists in a transvesical incision into the sphincter with enucleation of any periurethral adenomas that may be present.

Cancer.—Bumpus [41] reports 1,000 cases of carcinoma of the prostate seen at the Mayo Clinic prior to January, 1925. The average age of the patients was 65 years; in no case was it encountered before the forty-second year, and rarely before the forty-fifth year. In 485 cases in which no treatment was given, the average duration of the disease from the first symptoms to death was thirty-one months. When metastasis had occurred at the time of examination, two thirds of the patients died within nine months. When careful examination indicated that metastasis had not occurred, the average subsequent length of life was approximately one year. In 136 cases the urine was negative, and in 137 cases gross hematuria was noted; in 362 cases erythrocytes were found on microscopic examination. In 243 of 1,000 cases, metastasis was demonstrable. In 44 per cent it had affected the lymphatics. Five hundred and thirty-nine patients were examined roentgenographically, and the pelves of 123 and the spines of 107 were found to be affected,

40. Rubritius, H., and Schwarz, O.: Contribution to the Problem of Contracture of the Neck of the Bladder, J. Urol. **15**:461-466 (May) 1926.

41. Bumpus, H. C., Jr.: Carcinoma of the Prostate, Surg. Gynec. Obst. **43**:150-155 (Aug.) 1926.

making an aggregate of positive observations in approximately 25 per cent of the series. The femur of sixteen and the ribs of ten were affected, but always in conjunction with involvement of the pelvis. Of 246 cases in which roentgenograms were made of the lungs, they were diseased in twelve. In all of these, metastatic tumors were present in the spine or pelvis.

Of 178 cases in which prostatectomy was performed, there are completed records in 164 (92.1 per cent). In forty-seven a perineal operation was performed, and in 117 a suprapubic. The length of life following operation averaged thirty months for the group, nearly three times as long as when no treatment was given. Thirty-five of these patients are still alive, but half have not lived three years; of the seventeen others, twelve have lived more than five years and may be considered cured.

The clinical records of 112 cases treated with radium are reported. The dosage given averaged a little in excess of 2,000 milligram hours, and the patients lived an average of twenty-two months following their treatment. Of these, twenty-five are still living, nine more than three years, and four of these nine have lived more than five years. These results are about equal to those obtained by surgical treatment, considering that these cases were not as carefully selected. Just as the surgical results did not warrant the continuation of that form of treatment except in selected cases, so the results of radium treatment compelled its abandonment.

If, as is usually the case, there is only a small amount of residual urine present, its removal by the daily use of the catheter will probably be sufficient to maintain adequate renal function. If the obstruction is more complete and a catheter passes with difficulty, cystostomy is indicated. This was performed in 125 cases in the series, of which there are complete records of 117. The average duration of the disease was nearly twice as long, being fifty-seven months instead of the usual thirty months for patients who received no treatment. After operation these patients lived an average of twenty-four months, more than twice as long as the patients for whom cystostomy was not performed. Thirty-four are still alive, eleven more than three years after operation, and of this eleven six have lived more than five years.

Marion [42] divides prostatic cancer into two anatomic groups: the cancer "proprement dit" or glandular carcinoma, and the cancer resulting from the transformation of periurethral adenoma. The diagnosis is not difficult; it may be confused in rare cases with an unusual lesion: diffuse ligneous prostatitis. In the early stage the carcinoma may be

42. Marion, G.: A propos du traitement du cancer de la prostate, J. d'urol. méd. et chir. **21**:386-396, 1926.

mistaken for simple hypertrophy, but if the seminal vesicles are enlarged carcinoma should be considered. Hard nodules usually mean malignancy; irregular masses are rarely inflammatory in origin. The treatment varies following the operability or nonoperability of the tumor. The operability is defined by the absence of diffusion in the periprostatic and perivesicular tissues and of unexplained persistent pains. The so-called cancer originating in the gland itself is rare on account of the fact that patients usually seek relief only if there is pain, a late symptom in this type of cancer. The opposite is true for carcinoma originating in periurethral adenoma, which causes early dysuria and frequency. Both types of tumor should always be extirpated when possible. Definite cures are not frequent (three in forty-eight of Marion's private cases), but many patients (twenty-six out of forty-eight) keep regular function of the bladder up to the end. The operative mortality in Marion's cases was 10 per cent. All but 6 per cent of the patients that lived after operation derived some benefit from it. Marion uses the suprapubic route in removing malignant tumors of the prostate, believing that it is not more serious than the perineal operation and that it gives the patient immediate relief without the risk of fistula, other sequelae, or a long convalescence. The seminal vesicles should be removed with the prostate, and the catheter should not be inserted until from fifteen to twenty days after operation. Marion does not favor radium; he believes that even in inoperable cases the results are unsatisfactory. Cystostomy is indicated only when catheterization is difficult or has to be repeated frequently, or when it causes hemorrhage.

TESTIS

Orchidopexy.—Turner [43] describes the results of his operation for undescended testis. The operation is briefly as follows: A small incision is made in the external oblique muscle just above the internal abdominal ring. The internal oblique muscle is drawn upward, and the spermatic cord, enclosed with the patent funicular process in a sheath derived from the infundibuliform fascia, is exposed just below the internal ring. The spermatic cord and the testis are drawn out from the inguinal canal into the wound; the hernial sac, or the patent processus vaginalis, which is nearly always present, is separated from the vas and the veins after the fascial sheath has been opened, and is ligated above at the internal ring and below just above the tunica vaginalis. The facial sheath of the cord is divided, and the attachment of the gubernaculum to the tissues of the groin is torn through. The

43. Turner, Philip: An Analysis of the Results in Fifty Cases of Transseptal Orchidopexy for Imperfectly Descended Testicle, Guy's Hosp. Rep. **75**:209-221 (April) 1925.

gubernaculum, just below the testis, is transfixed and ligated; the ends of the ligature are left long and are secured by a pair of Spencer Wells forceps; the redundant portion of gubernaculum beyond the ligature is cut away. An incision is made on the opposite side of the scrotum, and a bed for the testis to be transplanted is made between the septum and the normally placed testis. The forceps with the ends of the ligature are introduced through the incision in the external oblique muscle and are directed along the inguinal canal, through the external ring, and well down into the scrotum; they are then made to impinge against the septum, which is pushed before them into the scrotal wound. A small incision is made in the septum over the points of the forceps, which are then pushed through, and the ends of the ligature are secured. The forceps are withdrawn slowly and are opened from time to time so as to make a way for the passage of the testis, which is drawn into its new position by traction on the ligatures.

Turner sets himself high standards and follows his cases thoroughly. In 70 per cent of his cases, the results were splendid. In 16 per cent they were poor, but by no means failures, and in 14 per cent atrophy and failure are recorded.

Cancer.—Handfield-Jones [44] reviews the work on chorionic carcinoma from the time of Sanger's first description of a chorionic epithelioma to the present time. Handfield-Jones states that certain definite histologic characteristics must be present to make a pathologic diagnosis. These elements are the syncytium, Langhan's cells, chorionic wandering cells and the masses of blood and fibrin. Chorionic carcinoma is highly malignant, producing widespread metastasis through the blood stream. The lungs are the usual site of deposit, the secondary deposits usually resembling the original growth. Dissemination may also occur by way of the lymphatics to the aorta and inferior vena cava. It is of interest to know that occasionally in the uterine cases there is spontaneous repression of the metastatic lesions with the removal of the primary growth. Attention has been drawn to the fact that in some cases there has been activity in the male breast in that it may enlarge and secrete colostrum. There are numerous theories regarding the site of origin; the generally accepted view is that it arises from some element in a teratoma and that the formation of true fetal membranes is not necessary.

[ED. NOTE.—Clinically these testicular tumors do not differ from other testicular malignant neoplasms. The general symptoms vary with the site of the metastatic tumors. By far the most common symptoms

44. Handfield-Jones, R. M.: Chorionic Carcinoma in the Testicle: With a Report of a New Case, Brit. J. Surg. **13**:606-620 (April) 1926.

of secondary localization are pulmonary: dyspnea and hemoptysis. The chorio-epitheliomatous portions of the tumors are hemorrhagic and necrotic; microscopic examination reveals Langhans' cells with islands of syncytium intervening; there usually are numerous irregular blood spaces lined with flattened syncytial plates distributed between the Langhans cells. Besides the usual alveolar arrangement, the Langhans cells are found in a more independent proliferation consisting of duct-like and complex papillary forms lining cystic spaces. Besides the chorio-epitheliomatous portions, teratomatous elements are found in about half of the cases.

The pathogenesis of these testicular growths is a disputed question, as is that of the other testicular malignant neoplasms. Chorio-epithelioma is trophoblastic and yet the presence of teratomatous elements must also be explained. Three possible points of origin have been suggested: (1) from interstitial cells of the testis, (2) from misplaced multipotential cells included during embryonic development, and (3) from the spermatogenic cells. The fact that no case occurring before puberty or after cessation of sexual activity has been seen, is used as an argument against the possible association with spermatogenesis. Ewing has suggested that it is hazardous to attempt the diagnosis of chorio-epithelioma of the testis in the absence of pulmonary or hepatic metastasis.]

SCROTUM

Tumors.—Rubaschow [45] states that tumors of the scrotum (skin growths excluded) are rare. They have the same characteristics as other tumors of the genital system; they are highly malignant and are, etiologically, difficult to classify. Rubaschow has divided these tumors into two main groups, the teratomatous or heterotopic tumors and tumors of the local tissues. Metastatic growths are not considered.

Under heterotopic tumors are included: (1) teratomas and dermoids, probably related to teratoma testis, and (2) mesodermal growths, thought to originate from the embryonic myotome and sclerotome, or possibly body rests carried down with the descent of the testis. The mesodermal tumors include myomas, fibromyomas, chondromas and osteomas, and are divided into four types: (1) fibromas with some smooth muscle; (2) chiefly myomatous tumors also containing some fibrous tissue, resembling the fibromyoma; (3) those with only muscle tissue, leiomyomas, and (4) those of embryonic striped muscle, rhabdomyomas. Genetically they are either teratomas with an excess of muscle tissue or they are of true mesodermal origin. Lipoma, sarcoma, angioma or lymphangioma may arise from other scrotal tissues.

45. Rubaschow, S.: Die Geschwülste des Hodensacks (Hautgeschwülste ausgeschlossen), Ztschr. f. urol. Chir. **19**:218-230, 1926.

Rubaschow found only thirty-eight scrotal tumors in fifty years. The majority were embryonic in origin; even the lymphangiomas may have their origin in embryonic anlagen which belong to the retroperitoneal tissues. In frequency of occurrence of tumors, the organs most frequently involved are the testis, cord, tunica vaginalis and scrotum, respectively.

ANESTHESIA

Arce [46] reports on the type of anesthesia used in the University Surgical Clinic in Buenos Aires. Lumbar anesthesia reduces the blood pressure and causes the patient to faint or collapse. To employ this type of anesthesia without danger to the patient in operations of the lower limbs, the perineum, the genito-urinary organs and the abdomen, the blood pressure must be within normal limits.

In operations on the scrotum, testes, penis and spermatic cord, Arce injects from 0.08 to 0.1 Gm. in the second lumbar space. In operations on the kidney and upper part of the abdomen, he injects 0.1 Gm. in the eleventh or twelfth dorsal space.

CHYLURIA

Kutzmann [47] reports a case of nonparasitic chyluria of three years' duration in a male negro, aged 21. The patient was later shown to have a perirenal abscess about the upper pole of the left kidney. The chyle came from this kidney, and the chyluria disappeared after nephrectomy.

In a review of the literature, an excellent discussion of the theories on nonparasitic or nontropical chyluria was found. This was advanced to explain this much misunderstood condition. The theories center around the supposition that the kidney through some abnormality of metabolism secretes or excretes the chyle which is abnormally present in the blood, and around a second and more feasible theory that there is some abnormal connection between the urinary tract and the larger lymph channels. Several instances of such abnormal communication having been demonstrated are cited. The route between the intestinal and the renal lymphatics is not well understood. According to Magnus-Levy, the chyle must first go through the mesenteric lymph channels to the mesenteric lymph nodes and thence to the thoracic duct. Thence, because of obstruction, there is a retrograde flow to the upper lumbar nodes, which drain the renal lymphatics. To obtain such a retrograde

46. Arce, José: Die Lumbalanästhesie in der Chirurgie, Deutsch. med. Wchnschr. **1**:644-646 (April 9) 1926.

47. Kutzmann, A. A.: Nonparasitic Chyluria, Ann. Surg. **82**:765-780 (Nov.) 1925.

flow an insufficiency of the valvular system of the lymphatics must be assumed. Assuming a lymphatic block in the renal lymphatic system, leakage of chyle may occur through the kidney. According to the researches of Stahr and Kumita, the lymph channels of the renal cortex can be injected from the capillary bed of the muscularis of the small intestine. Goebel states that to have chyluria, first, the lymph channels must open into the urinary tract and, second, the lymph channels must empty their contents through recurrent channels into these lymph channels of the urinary tract. Marion assumes a secretory and an excretory type of chyluria. Nearly all hypotheses are insufficient and little better than those advanced many years ago.

Nonparasitic chyluria is rare in America; it is more common on the European continent. More than 100 cases have been reported. It occurs chiefly during early and middle adult life; only twelve cases have been reported in children. Milky or turbid urine usually is the only primary symptom. This may be complicated by backache or renal colic. It may be constant or intermittent, and it may occur at different times of the day.

The urine has been the subject of much study. Usually, it will contain from 1 to 3 per cent of fat by Babcock's method. Occasionally erythrocytes or leukocytes may be found, fibrin clots are frequently found, and the urine often has a pinkish tinge. The differentiation from lipuria, such as is found in phosphorus poisoning, and degenerative renal processes, and from pyuria must be carefully made. The history of residence in tropical countries should lead one to suspect the parasitic or filarial form. Chyluria associated with diabetes, pregnancy, the puerperium, tuberculosis of the peritoneum and carcinoma in the region of the kidney has been noted.

The disease is one of long duration, and because of its benignity has a fair prognosis. One case of fifty-five years' duration is cited. Treatment is entirely empirical. A low fat diet has given good results in a number of cases. Renal lavage with weak solutions of silver nitrate may be tried. Fulguration or cauterization of demonstrable points of communication has been successful at times. Exploration of the kidney and nephrectomy have been performed in poorly progressing cases. Some observers have abolished the symptoms with neoarsphenamine.

[Ed. Note.—The obscurity that clouds the etiology of chyluria of any type makes its proper treatment difficult. More study of the relation of the renal lymphatic channels is necessary. Probably this condition frequently passes by undiagnosed in the course of routine clinical examinations. Murky urine which does not clear on heating or the addition of acid, and which contains no formed bodies, should lead to

investigation. The addition of ether will clear the specimen, and the fat thus may be obtained by extraction. The entire urinary tract should be thoroughly examined and a good general examination carried out to expose possible related pathologic changes. It would seem that conservative treatment with diet, lavage and the like should always be the first therapeutic effort. Operative treatment for such a condition alone seems radical and hardly indicated in uncomplicated cases.]